ANALYSIS OF SHORT TERM OUTCOME OF ACUTE KIDNEY INJURY NETWORK STAGE III OF ACUTE KIDNEY INJURY

Dissertation Submitted to
THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

In Partial fulfillment of the regulations
For the award of the degree of
D.M. DEGREE EXAMINATION
BRANCH NO. III, NEPHROLOGY

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI – TAMILNADU

AUGUST-2013

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my beloved Professor and Head of Nephrology Department, Dr. M. Edwin Fernando, M.D.D.M., for his motivation, advice, guidance and constructive criticism which enabled the completion of this work.

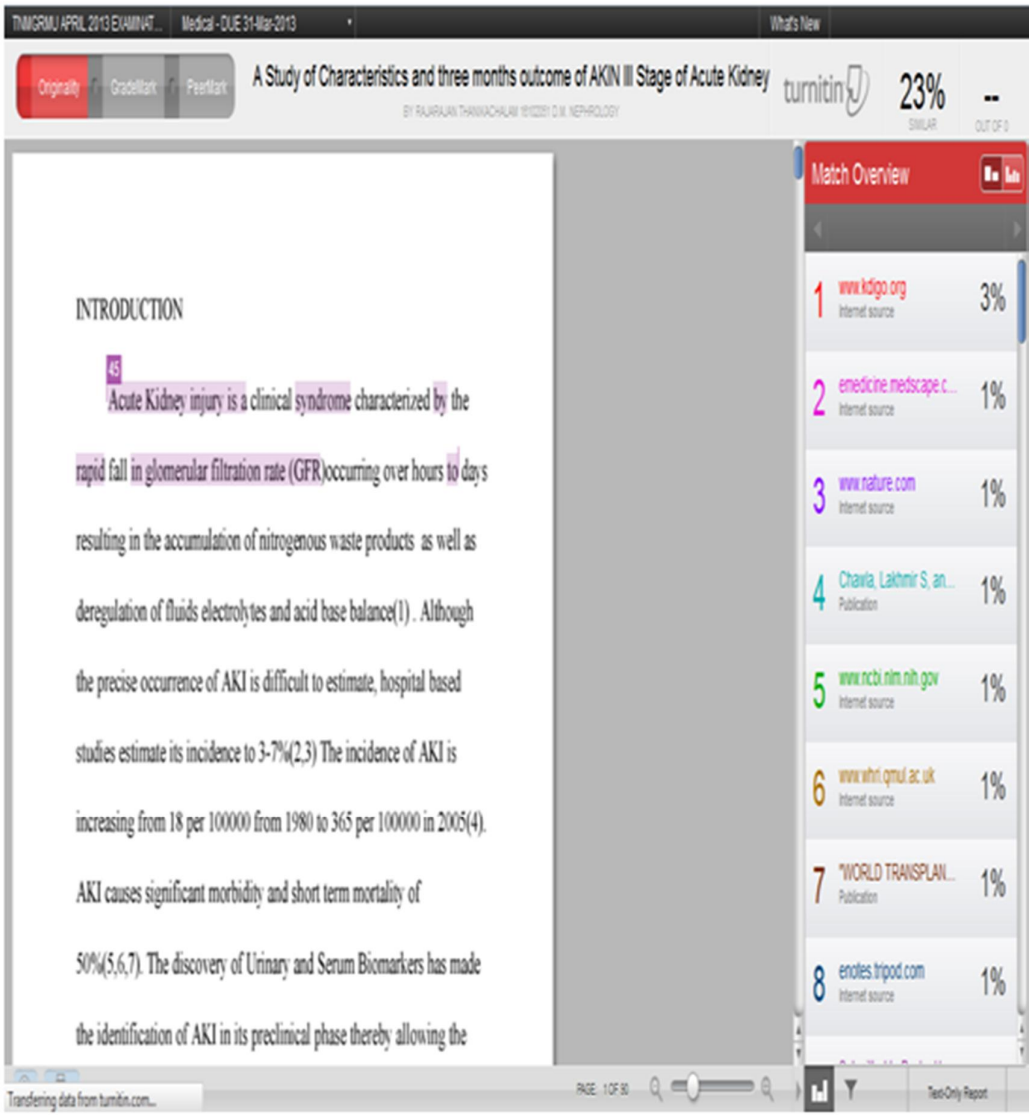
I am extremely grateful to Dr.R.Manorajan M.D.D.M. Dr. A. Ezhilarazi, M.D.D.M., Dr.S. Thirumavalavan, M.D.D.M., Dr.S.A.K. Noor Mohammed, M.D.D.M. Dr.Karunakaran M.D for their valuable guidance and Co-operation.

I thank Mr.Ravanan, Assosiate Prof. of Statistics, Presidency college, Chennai for the statistical guidance rendered and Mr.Sharath kumar for preparing the manuscripts. I render my sincere thanks to my collegues, Dr.R.P.Senthil kumar, Dr.M.Rajkumar for the support rendered to me in carrying out this work.

I extend my sincere gratitude to the staffs, Dialysis technicians, Students and ward assistants who helped me in various ways in carrying out this work.

I am extremely grateful to my family and the almighty for the moral support rendered throughout my life.

I am immensely thankful to the patients who have participated in this study.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A Study of Characteristics and three months outcome of AKIN III Stage of Acute Kidney
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INTRODUCTION
Acute Kidney injury is a clinical syndrome characterized by the rapid fall in glomerular filtration rate (GFR)occurring over hours to days resulting in the accumulation of nitrogenous waste products as well as deregulation of fluids electrolytes and acid base balance(1) . Although the precise occurrence of AKI is difficult to estimate, hospital based studies estimate its incidence to 3-7%(2,3) The incidence of AKI is increasing from 18 per 100000 from 1980 to 365 per 100000 in 2005(4). AKI causes significant morbidity and short term mortality of 50%(5,6,7). The discovery of Urinary and Serum Biomarkers has made the identification of AKI in its preclinical phase thereby allowing the
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This is to certify that this Dissertation titled **"ANALYSIS OF SHORT TERM OUTCOME OF AKIN III AKI"** is a bonafide work done by **Dr.T.RAJARAJAN,** Post Graduate Student (2010-2013) in the Department of Nephrology, Govt. Stanley Medical College, Chennai under the direct guidance and supervision and in partial fulfillment of the regulations laid down by the Tamilnadu Dr. M.G.R. Medical University, Chennai for DM Branch III, Nephrology Degree examination.

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DECLARATION

I **Dr. T. RAJARAJAN,** solemnly declare that this dissertation entitled**, "ANALYSIS OF SHORT TERM OUTCOME OF AKIN III AKI"** is a bonafide work done by me at the department of nephrology, Stanley Medical College and Government Stanley Hospital during the period 2010 – 2013 under the guidance and supervision of the Professor Dr. M. Edwin Fernando M.D. D.M., Head of the Department of Nephrology of Stanley Medical College and Government Stanley Hospital, Chennai.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of D.M. Degree (Branch-III) in Nephrology.

Place: Chennai

Date: 15-3-2013

Dr. T.RAJARAJAN

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INTRODUCTION

INTRODUCTION

Acute Kidney injury(AKI) is a clinical syndrome characterized by the rapid fall in glomerular filtration rate (GFR)occurring over hours to days resulting in the accumulation of nitrogenous waste products as well as deregulation of fluids electrolytes and acid base balance(1). Although the precise occurrence of AKI is difficult to estimate, hospital based studies estimate its incidence to 3-7% (2,3) The incidence of AKI is increasing from 18 per 100000 from 1980 to 365 per 100000 in 2005(4). AKI causes significant morbidity and short term mortality of 50%(5,6,7). The discovery of Urinary and Serum Biomarkers has made the identification of AKI in its preclinical phase thereby allowing the clinicians to aggressively intervene to prevent further damage. The burden of AKI lies not only in in-hospital mortality and morbidity, but also in its long term outcome of progression to Chronic Kidney Disease. A traditional concept of regarding renal outcome after an episode of AKI that 5%experience no recovery, 5% manifest progressive renal dysfunction has changed considerably now. Recent studies have shown 10-40% of dialysis requiring AKI remain dialysis dependent. Also it increases the risk of developing progressive CKD by 28 folds (8). Time has evolved now to view AKI as part of AKI-CKD syndrome were AKI brings out subtle renal abnormalities to the fore. To emphasis the above

mentioned points this study was done to analyze the characteristics and the short term outcome of severe AKI (AKIN stage III) patients admitted in Govt. Stanley Medical College and Hospital.

AIM

AIM

To analyze the characteristics and short term (three month) outcome in Acute Kidney Injury (Acute Kidney Injury Network Stage III).

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Although more than 30 definitions are available for the acute kidney Injury the following definition holds good for the better understanding of AKI

"It is a rapid decline in renal function over 48 hours as demonstrated by an increase in Serum Creatinine of more than 0.3mg/dl or more than 50% increase in base line serum creatinine or the development of Oliguria"(9).

AKI is a clinical syndrome of varying manifestations from completely asymptomatic to severe uremic symptoms due to the accumulation of nitrogenous waste products. No doubt it causes considerable morbidity and mortality to the patients. The burden of AKI not only mention the in-hospital mortality and morbidity but also with the long term outcome of dialysis dependency, risk of developing progressive chronic kidney disease and all cause of death.(5,6,7,8,10).

EPIDEMIOLOGY & CLASIFICATION:

The exact occurrence of AKI in the community and in hospital is not clear due to the application of varying criteria and definitions to diagnose AKI. To bring about uniformity and reproducibility of defining

AKI, Acute dialysis quality initiative group (ADOQI) in 2002 first proposed the consensus definition for AKI. It was named as RIFILE criteria with the classification scheme consist of three strata for its diagnosis (R, I, F) and two outcome stages (L&E) (11). The first strata give the highest sensitivity of diagnosing AKI and the third strata, the highest specificity.

RIFLE and AKIN Criteria for Diagnosis of AKI

RIFLE Classification[3]	GFR Criteria	Urine Output Criteria
Risk	S_{Cr} >1.5 x baseline or ΔGFR >25% reduction	UO <0.5 ml/kg/h x 6 h
Injury	S_{Cr} >2.0 x baseline or ΔGFR >50% reduction	UO <0.5 ml/kg/h x 12 h
Failure	S_{Cr} >3.0 x baseline or ΔGFR >75% reduction or S_{Cr} >4.0 mg/dl	UO <0.3 ml/kg/h x 24 h or anuria x 12 h
Loss	Persistent acute renal failure = Complete loss of function for >4 wk	
ESRD	End-stage renal disease > 3 months	

Recently AKIN (Acute Kidney Injury Network) has come up with the modifications of RIFILE criteria which comprise R, I&F criteria with the addition of increase in serum creatinine of ≥ 0.3 mg/dl to the RISK ® class(12).

AKIN Classification [6]		
Stage	Serum Creatinine Criteria	Urine Output Criteria
1	$\Delta S_{Cr} \geq 0.3$ mg/dl (30µmol/l) or $S_{Cr} \geq 1.5, \leq 2.0$ x baseline	UO < 0.5 ml/kg/h x 6 h
2	$S_{Cr} > 2.0, \leq 3.0$ x baseline	UO < 0.5 ml/kg/h x 12 h
3	$S_{Cr} > 3.0$ x baseline or $S_{Cr} \geq 4.0$ mg/dl with an acute rise ≥ 0.5 mg/dl (50µmol/l) or on renal replacement therapy	UO < 0.3 ml/kg/h x 24 h or anuria x 12 h

Small but important difference exists between the two classifications.

1. The time constraint of 48 hours for the diagnosis of AKI is required in AKIN criteria in contrary to RIFLE criteria of 7 days

2. GFR is taken into consideration for RIFLE criteria.

3. RIFLE classes I & E are not reported in AKIN stages

4. Both the systems utilize serum creatinine and urine output criteria. Only one criteria has to be meet to qualify for the given class and stage of AKI.

5. Dialysis requiring AKI is placed in AKIN stage III irrespective of Serum Creatinine or Urinary abnormalities.

LIMITATION OF BOTH THE SYSTEMS

1. Unable establish the concordance between serum creatinine and urine output even with mortality risk.

2. Poor correlation between GFR and AKI stages.

3. Excessive reliance of base line creatinine which in many times are unavailable.

4. Relative changes in Sr. creatinine to the time required to attain the fixed percentage depend upon baseline renal function.

After the advent of these two major systems, the physician community has gone a bit closer to precisely estimate the incidents of AKI. Recent estimation showed that 3-7% of hospitalized patients develop AKI as to 25-30% of the ICU patients (2,3). Requirement of RRT is 5-6%. As per national hospital discharge survey in the US, there were increased hospital discharges from dialysis requiring AKI, from 18/100000 in 1980 to 365 /100000 in 2005(13). Also dialysis requiring AKI are also on the rise with the increase from 322.7-522.4 per 100000 person years from 1996 – 2003(14).

ETIOLOGY OF AKI

It is traditionally classified as Pre renal, Intrinsic renal and Post renal AKI for the diagnostic approach. Even though there maybe overlap among the components.

PRE RENAL AKI:

It is the most common cause of AKI accounting for 40-55%. It is the easily reversible form of AKI resulting from hypo perfusion of the kidneys resulting from decreased in effective arterial volume. Although reversible, prolonged hypo perfusion to kidneys may result in parenchymal damage and eventually resulting in intrinsic AKI.

***Causes of Pre renal AKI*:**

***Volume depletion*:**

- Renal losses - Diuretics, polyuria
- GI losses - Vomiting, diarrhea
- Cutaneous losses - Burns, Stevens-Johnson syndrome
- Hemorrhage
- Pancreatitis

***Decreased cardiac output* :**

- Heart failure
- Pulmonary embolus
- Acute myocardial infarction
- Severe valvular disease

***Systemic vasodilatation*:**

- Sepsis
- Anaphylaxis
- Anesthetics
- Drug overdose

***Afferent arteriolar vasoconstriction*:**

- Hypercalcemia
- NSAIDs, amphotericin B, calcineurin inhibitors, nor epinephrine, radio contrast agents
- Hepato -renal syndrome

***Diseases that decrease effective arterial blood volume*:**

- Hypovolemia
- Heart failure
- Liver failure
- Sepsis

Hypovolemia results in the activation of baroreceptors and osmotic center in the brain leading to the production and release of catecholamine and ADH respectively. Increase in the intra renal activity of angiotensin II secondary to hypovolemia to maintain GFR becomes maladaptive when the volume depletion prolongs (15). Local myogenic reflex to maintain GFR by selectively dilating afferent arteriole fails when the mean systemic arteriolar blood pressure falls below 75-80mmHg. Although these compensatory mechanisms act in concert to prevent AKI they both are overcome when the state of hypo perfusion prolongs, eventually resulting in pre renal AKI. Pre renal AKI in turn pre disposes the patient to Acute Tubular Injury (Intrinsic AKI).

INTRINSIC AKI:

The causes of the intrinsic AKI can be divided based on the various renal components viz., large vessels, micro vasculature, tubule interstitium and glomeruli. It is the second most common cause of AKI.

***Etiology of Intrinsic renal AKI*:**

- Renal artery obstruction - Thrombosis, emboli, dissection, vasculides
- Renal vein obstruction - Thrombosis
- Microangiopathy - TTP, HUS, disseminated intravascular coagulation (DIC), preeclampsia
- Malignant hypertension
- Scleroderma renal crisis
- Transplant rejection
- Atheroembolic disease

Glomerular causes:

Anti-glomerular basement membrane (GBM) disease - Goodpasture syndrome or renal limited disease

- ANCA-–associated glomerulonephritis (ANCA-associated glomerulonephritis) - Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis

- Immune complex glomerulonephritis - Lupus, post infectious glomerulonephritis, cryoglobulinemia, primary membrano-proliferative glomerulonephritis.

Tubular etiologies:

- Rhabdomyolysis, intravascular hemolysis

- Tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate

- Aminoglycosides, lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, radiocontrast agent

Interstitial nephritis causes include the following:

Penicillin, cephalosporin, NSAIDs, proton-pump inhibitors, allopurinol, Rifampin, indinavir, mesalamine, sulfonamides

Pyelonephritis, viral nephritides

Systemic disease - Sjögren syndrome, sarcoid, lupus, lymphoma leukemia, TINU Syndrome.

POST RENAL AKI:

It is caused by the obstruction to either ureter, bladder or urethra . It accounts for < 5% of AKI initially increased intra tubular pressure is compensated by the decrease in afferent renal arteriolar vasodilatation so as to maintain single nephron GFR (SNGFR). Later after 24 SNGFR falls rapidly as a result of progressive rise in intra tubular pressure unattended by the static afferent arteriolar tone.

***Causes of post - renal AKI*:**

- Stone disease
- Stricture
- Intraluminal, Extraluminal, or intramural tumors
- Thrombosis or compressive hematoma
- Fibrosis

PATHOPHYSIOLOGY OFAKI:

The understanding of the pathophysiology of renal diseases is well characterized by the animal models. Ideal models should have reproducibility, clinical relevance, therapeutic value, possibility of study of mechanism to have control over extrinsic factors and isolation of

single variables. Unfortunately none stood because AKI has multi factorial etiology and most of the humans have premorbid illness. The hypo perfusion / cardiac arrest model for ischemic AKI and cecal ligation and puncture (CLP) for septic AKI are considered to be closely associated with human counterpart (16,17,18,19). Although all segments of nephron can undergo injury during ischemic insult, epithelial cells especially of S3 segment are the most vulnerable,(20) followed by endothelial cells(21). Proximal tubular cell injury results in drop in GFR through afferent arteriolar vasoconstriction primarily mediated through proximal tubular obstruction and tubule glomerular feedback (22,23). Even though proximal epithelial cells burn much of the injury in the early phase, there occurs a cross talk between the epithelial and endothelial cells mediating final insults like vasoconstriction, tubular cell apoptosis, necrosis, inflammation. Sub lethal injury to epithelial cells lead to actin cytoskeleton disruption causing detachment of microvilli, membrane bound extra cellular vesicles or blebs (24), loss of basolateral tight junction(25), redistribution of Na / K ATPase and integrins to apical location(26) and cast formation. Lethal injury produces apoptosis and necrosis of epithelial cells. Number of potent mediators of inflammation like TNF-α, IL-6 , IL-8 ,MCP, TGF-β are secreted by injured proximal tubular epithelial cells(27) as do TLR-2,

C5&C4(28), causing parenchyma inflammation and subsequent damage. Endothelial dysfunction causes continued ischemic renal insult; hence it is rightly termed as the Extension phase of AKI. With ischemia, renal vascular bed shows vasoconstriction probably as the result of imbalance between eNOS and iNOS (29) followed by the disruption in actin cytoskeleton causing endothelial swelling and increased permeability (30), activation of coagulation cascade, consumption of protein C, and thrombomodulin (31). Endothelial dysfunction also causes inflammation through leukocyte recruitment (32), erythrocyte trapping and roulex formation (33). Due to the better understanding of the pathogenesis in AKI, various experimental therapies were tried in animal models to halt its progression including CD133+ progenitor / stem cells, mesenchymal stem cells, VEGF, endothelial progenitor cells (CD 34, 133, VEGF receptor 2)

CLINICAL ASSESMENT & DIAGNOSIS:

Pre renal AKI should be suspected if there is evidence of intra vascular volume depletion like sense of thirst, orthostatic hypotension and tachycardia (postural drop in diastolic BP >10 mmHg and tachycardia > 10 beats/ min), decreased jugular venous pressure, diminished skin turgor, absence of auxiliary sweat. Volume

unresponsive pre renal AKI may be suspected in patients with CCF, liver disease, Nephrotic syndrome with the evidence of pedal edema pulmonary congestion, cardiomegaly, elevated JVP. Intrinsic renal AKI should suspected in euvolemic renal failure with varying symptoms with respect to renal compartments affected. Flank pain, nausea, Hematuria, cutaneous nodules, lividoreticularis, absent peripheral pulses, cholesterol plaques in the retina. Nephrotoxic ATN can be diagnosed with reviewing of pharmacy prescriptions, radio contrast exposure and native medicine intake. Pigment ATN should be suspected in the setting of rhabdomyolysis and haemolysis. Acute interstitial nephritis is evident from the recent exposure of drugs, maculopapular rashes, arthralgia and Eosinophilia. Primary and secondary glomerular diseases as a cause of AKI should be entertained in the presence of Glomerular Haematuria, proteinuria along with or without the features of extra renal features like rashes arthralgia, neuropathies, fever, etc., Post renal AKI usually present with anuric renal failure but a pattern of fluctuating urine output is not unusual. Presence of suprapubic flank pain, palpable bladder by abdominal examination and enlarged prostrate by pre rectal examination should point towards its diagnosis.

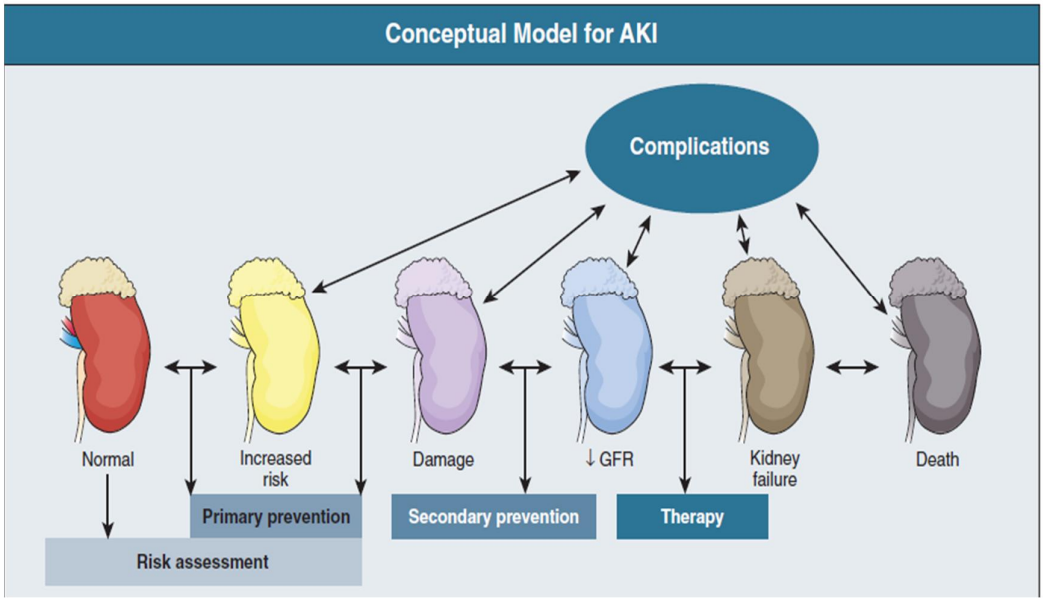
LABORATORY INVESTIGATIONS:

Urine analysis has always been a strong point in diagnosing various etiologies of AKI. Presence of normal or few RBC and WBC in urine suggest Pre renal and Post renal AKI. Presence of granular casts suggests acute tubular necrosis, RBC casts in vasculides, Glomerulonephritis and WBC casts in interstitial nephritis and acute pyelonephritis. Eosinophilia usually suggests atheroembolic renal disease and acute interstitial nephritis. Crystalluria occurs in drugs like sulfonamides, acyclovir, indinavir, acute urate nephropathy and radio contrast exposure. The application of FeNa to distinguish pre renal and intrinsic renal AKI has gone to disrepute in view of overlapping values in both these conditions. Urine, uric acid / creatinine ratio> 1 suggest tumor lysis syndrome or acute urate nephropathy. Radiological imaging is most important in diagnosing post renal AKI which includes plain radiography, ultrasonogram, Computed Tomography, MRI & antegrade and retrograde pyelography.

URINARY BIOMARKERS:

Biomarker is defined as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes,

pathogenic processes or pharmacological responses to therapeutic interventions (33).



The advent of biomarkers has made the diagnosis of AKI at the damage stage of the conceptual model. Urinary biomarkers that are detected in the AKI patients are either specifically produced by the injured proximal tubular cells or due to the failure of proximal tubular cells to absorb the specific filtered proteins. Numerous novel biomarkers are being discovered for clinical application in AKI detection, especially post operative AKI.

The following are significances are attributed to the urinary biomarkers:

1. Predicts AKI much earlier than elevation of serum creatinine (34,35,36).

2. Intensity of elevation is correlated with the need for dialysis, death and duration of hospital stay(37,38)

3. Detection in the urine till the renal recovery is complete.

The list of tubular injury biomarkers is increasing as time rolls on. The list includes α1 Microglobulin, β2- Microglobulin, glutathione, S-transferase, IL-18, KIM-1, liver type fatty acid binding protein, netrin-1, NGAL, NAG and Urinary cystatin-C. Of these, KIM-1, NGAL, NAG has more sensitivity and specificity (80-95%) (34).

COMPLICATION OF AKI :

It includes hyperkalemia, metabolic acidosis, volume overload, cardiac complications like arrhythmia, myocardial infarction and pulmonary embolism, Anemia, Platelet dysfunction, Clotting factor abnormalities, Infections (most common and serious complication) (39), Pericarditis, Uremic encephalopathy, Malnutrition and GI bleed. Recovery phase of AKI is complicated by volume depletion, hypernatremia, hypokalemia, hypomagnesaemia, hypophosphatemia and hypocalcaemia.

MANAGEMENT:

GENERAL PRINCIPLES:

1. It includes early goal targeted volume replacement to pre defined hemodynamic targets (MAP >65mmHg), CVP-10-12mmHg, target urine output more than 0.5 ml/kg/hour, central venous oxygen saturation >70% with the usage of combined crystalloids, blood transfusion and vasopressors (40).

2. Intensive blood sugar control of 80-110 mg/dl using insulin therapy (41).

3. Avoidance of nephrotoxic agents and drugs that interfere with the compensatory mechanisms during renal hypo perfusion like amino glycosides, diuretics, NSAIDS, ACEI and ARBs(42).

Medical therapy with low dose dopamine, fenoldopam, ANP, mannitol & loop diuretics are not effective in reducing the need for replacement therapy or mortality (43,44,45,46,47).

RENAL REPLACEMENT THERAPY (RRT):

Apart from the traditional and absolute indications for renal replacement therapy in AKI much debate has already underway

regarding the timing of initiation of dialysis, modality and frequency of RRT. RRT in AKI includes intermittent hemodialysis (IHD), Continuous renal replacement therapy (CRRT), Hybrid therapies and Peritoneal dialysis. Single randomized controlled trial regarding the early initiation of RRT in AKI did not show any benefit in mortality or early recovery (48) . Two randomized controlled trials comparing CRRT and IHD, showed no differences in in-hospital and 30 days mortality rate (49,50). The VA / NIH and RENAAL trials to assess the outcome of more intensive dialysis (IHD 6 times / week and CRRT 35ml/kg/hour) over less intensive arm (3 times a week and CRRT 20ml/kg/hour) did not show any significant benefit for more intensive arm(51,52). Peritoneal dialysis (PD) is always being an option for patients who don't have access for IHD or CRRT with studies showing lesser efficacy in terms of metabolic control for PD over others (53), although a study from Brazil has showed equal efficacy against its counter parts(54).

OUTCOMES OF AKI

The short term mortality in intrinsic AKI is around 50 % (5,6,39,55). Although this figure may vary depending upon various etiologies, septic AKI causes 60-90% mortality and obstetric AKI 15%

(5,56,57). The overall 60 days and 90 days mortality rates were 52.6% and 44.7% respectively as per VA/NIH and RENAAL trials. The dialysis dependency rates following AKI varies from 10-40% (51,52,58). Ishani et al, recently reported that AKI was independently associated with three fold increased risk of developing ESRD (59). The long term five year follow-up study by Schiffl and Fischer enrolling 425 patients treated with RRT found that 43% of patients had partial renal recovery fulfilling stage 2-4 CKD (60). After one year, 27% had meaningful improvements with 8.2% fully recovering, 10% worsened renal function at five years. The prevalence of CKD among survivors was 14% with only 2% of survivors reached ESRD at five years.

The mechanism of progression of AKI chronic kidney disease could be explained by remnant kidney animal model where by the nephron loss from AKI result in hyper filtration, intra renal hypertension, tubular hypertrophy, attending arteriosclerosis, tubulo interstitial fibrosis and eventually glomerulosclerosis(62). The trigger of inflammation by proximal tubular cell injury leads to interstitial cell infiltration initially by neutrophils and later on by the monocytes – lymphocytes which in turn mediates interstitial fibrosis through the activation of cytokines like TGF-β, IL6, TNF α, MCP1, IL1β (27) . The endothelial injury contributes to the maintenance phase of AKI. The

vascular restorative capacity after AKI is decreased leading to significant decrease in blood vessel density (around 30-50% of normal) known as vascular dropouts (61). The reason for the vascular dropouts include ischemia induced inhibition of vascular endothelial growth factor (VEGF) and the induction of ADAMTS1 (62, 63). This reduction of micro vascular density activates the hypoxia induced pathways leading to progressive inflammation and downstream fibrosis. This mechanism of deficient VEGF induced vascular dropouts ultimately dictates the progression of CKD. This has made to employ VEGF as a treatment to prevent the progression to CKD. In experimental models this compound has ameliorated vascular dropouts if administrated in the immediate post injury period (64).

The traditional concept of AKI being a benign disease with only 5% progresses to CKD has been changed with the advent of wealth of information supporting its high rate of progression to CKD.

MATERIALS AND METHODS

MATERIALS & METHODS

STUDY DESIGN: A prospective analytical study.

STUDY DURATION: January 2012 to December 2012

SETTING: Government Stanley Medical College and Hospital, Chennai.

PARTICIPATING DEPARTMENTS: Departments of Nephrology, General medicine, General Surgery, Surgical Gastroenterology & Intensive Medical Care Unit.

STUDY POPULATION:

Patients admitted or developed Acute Kidney injury with Serum Creatinine ≥ 3.0 mg/dl and/or Anuria for 12 hours.

INCLUSION CRITERIA:

The patients who got admitted (or) developed AKI with Serum Creatinine ≥ 3.0 mg/dl and/or anuria of ≥ 12 hours.

EXCLUSION CRITERIA

AKIN I & II AKI, Preexisting Systemic hypertension, Diabetes mellitus, Previous Renal disease, Decompensated liver disease, Obstructive uropathy.

MATERIALS:

Complete blood count (which includes blood hemoglobin, total and differential WBC count, platelets counts and erythrocyte sedimentation rate (automated hematology analyzer)

1. Random blood sugar by – GOD-PAP method.
2. Blood urea – GIDH method
3. Serum Creatinine by Jaffe's method
4. Serum sodium by Ion specific electrode
5. Serum potassium by ion specific electrode
6. Sr. Bilirubin by Biuret method.
7. Sr. SGOT by IFCC method
8. Sr. SGPT by IFCC method
10. Sr. alkaline Phosphatase by IFCC method.
11. Sr. Protein by Biuret method
12. Sr. Albumin by BCH method

13. Urine analysis – dipstick and direct microscopy for formed elements

14. Spot urine Sodium by ion specific electrode.

15. Spot urine Creatinine by Jaffe method.

FeNa was calculated by the formula :

Urine Na / Serum Na x Serum Creatinine/ Urine Creatinine

16. Spot Urine protein by

Spot Urine PCR>0.3 was considered abnormal protein excretion.

17. Serum C3 – Immunoturbidometry

18.Serum C4 - Immunoturbidometry

19.ANCA - Immunofluorescence assay with ethanol fixed neutrophils.

20.ASO titre – Immunoturbidometry

21.Peripheral smear for malaria parasite or Quantitative buffy coat for P.Vivax.

22.Microscopic slide agglutination test or IgM ELISA (enzyme linked Immunosorbant assay) for leptospirosis.

23Culture studies which include urine, sputum & blood

24.Ultrasonography of abdomen and pelvis.

25.Plain Xray chest and plain X ray KUB (kidney, ureter & bladder) if required.

26.Renal biopsy was done with 18 Gauge, 20 cm BARD Biopty gun. Two linear cores were taken. One of the cores was processed in 10% formalin for the purpose of light microscopy and the other with Michelle's solution for Immunofluorescence study. For the light microscopy, the stains used were Eosin and Haematoxylin, Periodic acid Schiff, Mason trichrome and silver methenamine. Immunofluorescence study was done for IgG, IgM, IgA, C1q, fibrinogen, kappa and lambda light chains.

27.Glomerular filtration rate was estimated using Cockcroft-Gault equation.

eGFR $\geq$ 90ml/min was considered as normal renal function and eGFR < 90 ml/min as abnormal.

METHODOLOGY:

All patients who were admitted or developed Acute Kidney Injury with serum Creatinine >3.0 mg/dl in any of the wards in Government Stanley Hospital were identified. Patients were included based on strict inclusion and exclusion criteria.

Patients clinical characteristics were studied including age, sex, Oliguria/anuria, volume overload, hypotension, uremic symptoms like encephalopathy, pericarditis etc., were studied. Lab parameters that were taken into consideration were Hemoglobin, Presentation urea and creatinine, Peak urea and creatinine during hospital stay, Presentation and discharge urine analysis, Discharge urea and creatinine.

The patients were managed with RRT (Renal replacement therapy) if:

1. Volume overload features.
2. Hyperkalemia.
3. Uremic encephalopathy.
4. Uremic symptoms like pericarditis, bleeding diathesis.
5. Anuria >12 hrs or prolonged Oliguria.
6. Severe metabolic acidosis.

Renal biopsy was done in patients with:

1. Unexplained AKI.

2. Active urinary sediments with glomerular haematuria or proteinuria.

3. In case of suspected ATN, if renal function didn't improve after 3 weeks.

The patients were discharged either at clinical recovery or after stabilization of renal function.

The surviving AKI patients were followed up after 3 months for thorough clinical examination and lab investigations which included urine analysis, spot urine PCR, Blood urea, Serum creatinine. GFR was estimated through cockgraft-gault formula.

Renal biopsy was done only if there was proteinuria and/or hematuria and/or renal dysfunction at the follow up.

The presence of either proteinuria or hematuria or renal dysfunction at 3 months follow up was considered abnormal and these patients were considered to have persistent renal damage and probably chronic kidney disease. The outcome of AKI at 3 months was observed.

The risk factors for the presence of proteinuria/hematuria/renal dysfunction/overall abnormalities were studied.

DEFINITIONS :

- Old age was defined as age above 50 years.
- Anemia was defined as blood hemoglobin less than 11 gm/dl.
- Volume overload was defined as the presence of edema and/or elevated JVP and/or hypertension and/or pulmonary edema.
- Proteinuria was defined as urine PCR >0.3.
- Hematuria was defined as dipstick positive for blood.
- Renal dysfunction was defined as the presence of eGFR <90 ml/min.
- Overall urinary abnormalities were defined as the presence of Proteinuria and/or hematuria and/or renal dysfunction.

STATISTICAL METHODS:

The Pearson chi square test was used for independent variables. Sample T Test was used for the comparison of mean variables. Multiple logistic regression analysis was done for multivariate analysis. All analysis was done through SPS software version 17.0.

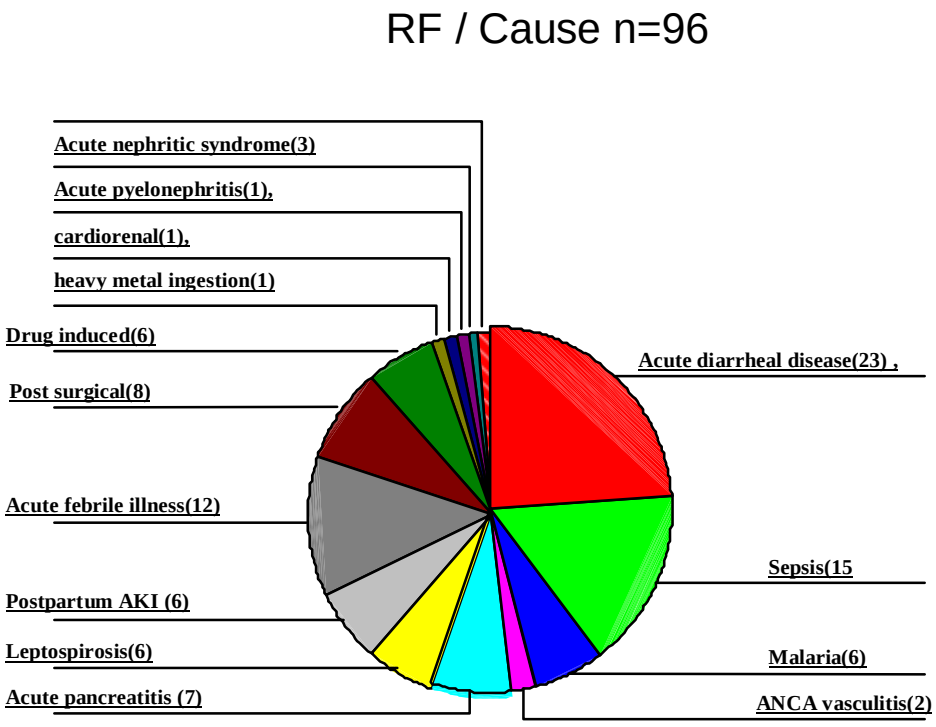
RESULTS

RESULTS:

Overall 96 patients were enrolled in the study after thoroughly executing inclusion and exclusion criteria's. 60 were male ad 36 were female. Male: Female ratio was 1:6:1.

Age of the patients varied between 14-66 years. Median age was 36 years. For the purpose of better statistical analysis, age more than 50 years was considered as old age. 29 patients constituting 30.2% belong to this group.

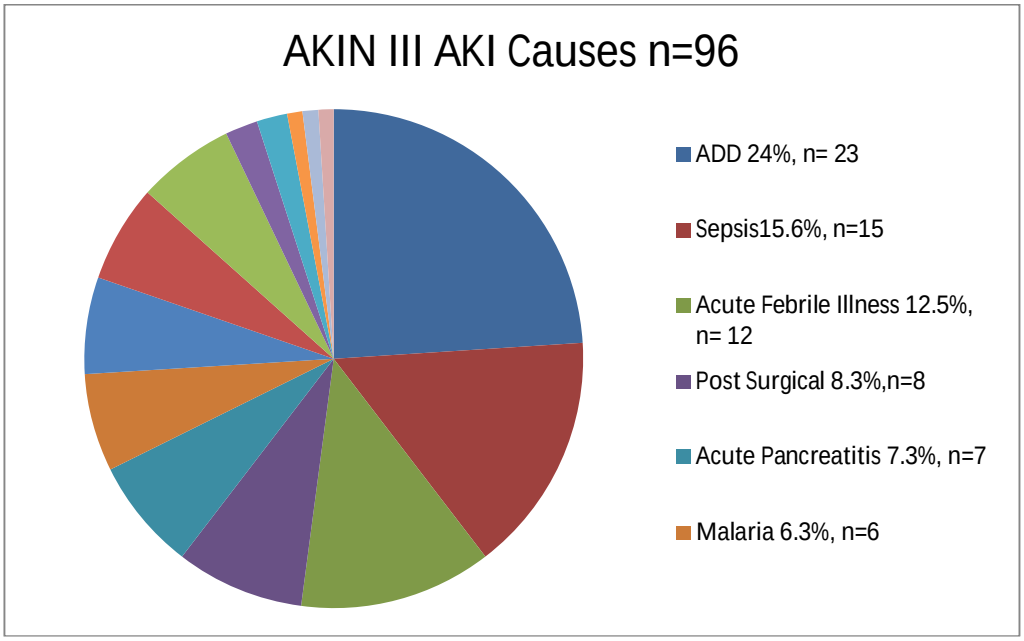
CAUSES OF ACUTE KIDNEY INJURY



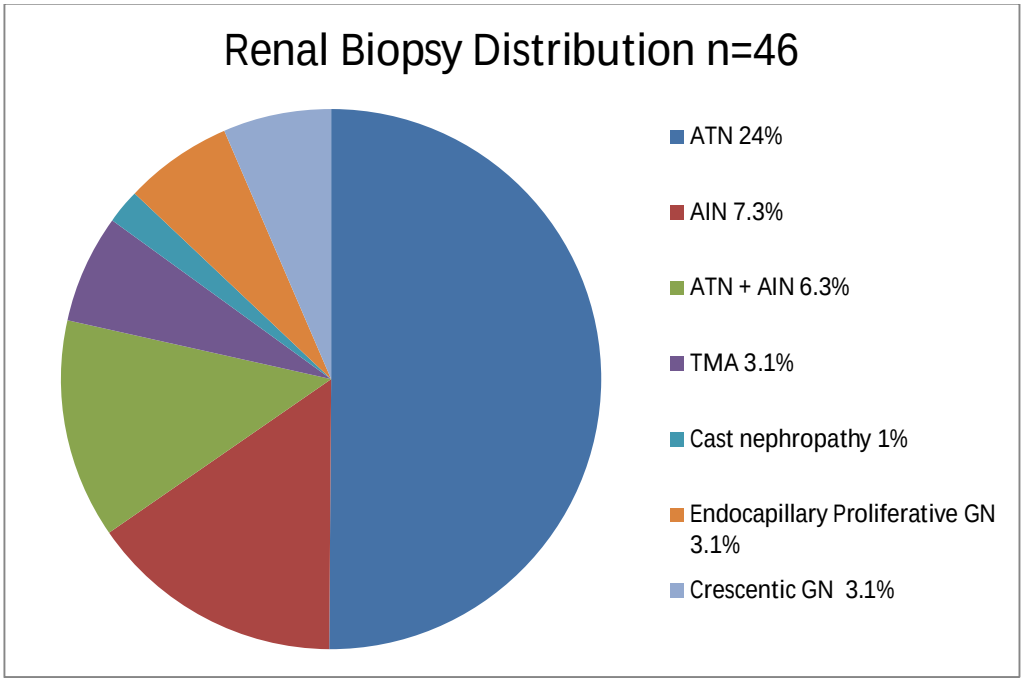
At presentation Oliguria/ anuria was present in 68 patients (70.83%). Volume overload state was present in 23 patients (23.95%). Hypotension was found in 6 patients (6.25%). Anemia was present in 64 patients. The mean blood hemoglobin was 10.5 ± 2.29 g/dl. The mean Serum Creatinine at presentation was 5.2±2.9 mg/dl. The mean peak Serum Creatinine during hospital stay was 7.2±3.14 mg/dl.

The mean blood urea at presentation was 135 ± 66.75 mg/dl. The peak blood urea during the course of hospitalization was 162 ± 60.8 mg/dl. Hyponatremia was present in 52 patients (54.1%). The mean serum sodium level was 133 ±13.95 mEq/dl. Hyperkalemia was detected in 12 patients (12.5%). The mean Serum potassium was 4.1 ± 1.03mEq/dl. Proteinuria was found in 49 patients (51.04%). Haematuria was found in 55 patients (57.29%). The combined urinary abnormalities (hematuria and / or proteinuria) were present in 70 patients contributing to 72.91% of the patient population.

Distribution of Causes of AKIN III AKI



Renal Biopsy in AKIN III AKI



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Renal Biopsy distribution:

	Frequency	Percent	Valid Percent	Cumulative Percent
Nil	50	52.1	52.1	52.1
ATN	21	21.9	21.9	74.0
AIN	7	7.3	7.3	81.3
ATN	2	2.1	2.1	83.3
TMA	3	3.1	3.1	86.5
Cast nephropathy	1	1.0	1.0	87.5
Endocapillary GN	3	3.1	3.1	90.6
Crescentic GN	3	3.1	3.1	93.8
ATN+AIN	6	6.3	6.3	100.0
Total	96	100.0	100.0	

63 out of 96 patients underwent Renal Replacement Therapy (RRT) out of which 62 underwent intermittent Hemodialysis (IHD) and 1 had Peritoneal Dialysis (PD).

The indications for RRT were:

Volume overload – 46,

Uremic encephalopathy – 13,

Prolonged Oliguria / anuria – 4,

Hyperkalemia–12.

Number of HD sessions varied between 2– 22. The mean number HD sessions were 8 ± 3.14. All IHDs were done with double lumen temporary catheters (14 cm, 13.5 Fr). Access vein used were internal jugular vein in 60 patients (96.77%), two patients had right subclavian vein (3.22%). The mean number of days of HD initiation from the days of detection of Acute Kidney Injury was 3±2.29 days, with the range of number of days varied from 1-11 days. Peritoneal Dialysis was done in one patient with rigid temporary PD catheter. The lone patient received 60 cycles and recovered completely. 33 patients were managed conservatively (34.37%).

The table comparing the characteristics of RRT and conservative groups:

Characters	RRT (n=63)	Conservative group(n=33)	P value
Age (yrs)	38.13±14.47	41.03±12.91	0.340
Hemoglobin(g/dl)	10.06±2.05	11.40±2.55	0.005
Oliguria / anuria	52	16	0.002
Mean presenting Creatinine (mg/dl)	5.72±3.02	4.26±2.08	0.021
Mean peak creatinine (mg/dl)	8.32±3.02	5.079±2.19	<0.001

Mean presenting urea(mg/dl)	143±63.25	121±71.74	0.021
Mean peak urea(mg/dl)	175.79±51.17	134.58±68.93	0.001
Mean Serum Na+ (mEq/dl)	133.09±6.6	133.8±7.72	0.640
Mean Serum K+(mEq/dl)	4.1±1.01	4±1.03	0.126
Discharge Serum Creatinine	2.32±1.22	1.72±0.68	0.015
Discharge Urine abnormalities	38	10	0.018
Mortality	3	3	0.694
Proteinuria at 3 months	11	1	0.72
Haematuria at 3 months	19	3	0.042
Renal dysfunction at 3 months	17	2	0.031
Abnormal Renal biopsy at 3 months	12	1	0.030

Mortality occurred in 6 patients (6.25%) . All the 3 patients in the conservative group were presented with multi organ dysfunction and very sick.

At discharge, renal dysfunction defined as GFR < 90 ml/min by Cockcroft- Gault formula was found in 70 patients (77.77%). Among them mild to moderate Renal failure (GFR >30 ml/min) was found in 36 patients (51.42%). Severe renal failure (GFR ≤ 30ml/min) was found in 34 patients (48.57%). Mean Serum Creatinine at discharge was 2.11±1.1 mg/dl. Urinary abnormalities were present in 47 patients (48.95%). The overall discharge abnormalities were found in 79patients (87.77%).

At follow up after 3 months of all the surviving patients normal renal functions defined as GFR > 90 ml/min was presenting 72 patients (66.66%). Renal dysfunction (GFR< 90 ml/min) was found in 18 patients (33.34%).

The breakup of patients with various ranges of GFR:

GFR 60-90 ml/min	9 (26.6%)
GFR 30-60 ml/min	2 (3.33%)
GFR < 30ml/min	7(30%)

Among the group with GFR < 30 ml.min, 5 patients were in Dialysis dependent Renal Failure and the other two were Dialysis Independent. Isolated urinary abnormalities without renal dysfunction were detected in 10 patients (16.66%). The overall follow up abnormalities was found in 30 patients (33.33%). The follow up renal biopsy were done in 19 among the 30 patients who fulfilled the criteria of renal biopsy (Hematuria and/or proteinuria and/or Renal dysfunction). Among the left out 11 patients, 5 patients were in Dialysis dependent renal failure and the other 2 had severe renal failure with smaller sized kidneys. Biopsy was deferred in them. The four patients with overall abnormalities refused renal biopsy. Among them one had renal dysfunction alone. The rest three patients had microhematuria alone.

The initial histopathology of dialysis requiring renal failure patients were:

Cast Nephropathy -1

Thrombotic microangiopathy with acute cortical necrosis - 2

Crescentic glomerulonephritis - 2

Acute interstitial nephritis -1

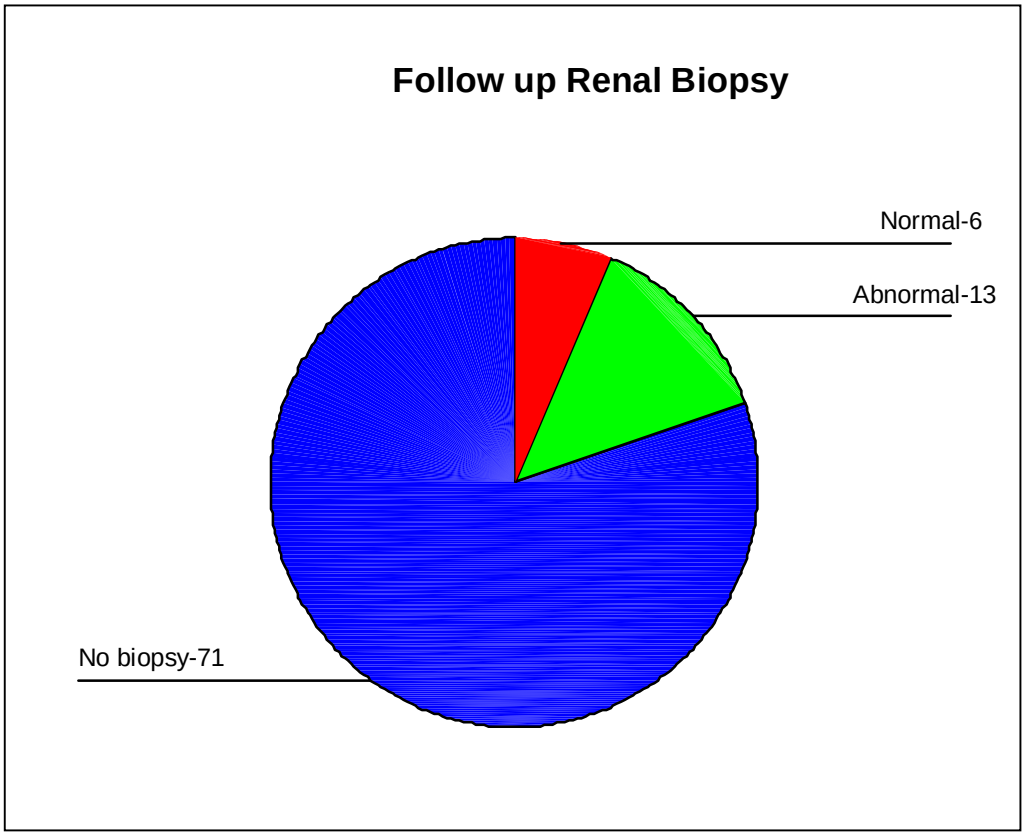
Biopsies of severe renal failure not required dialysis:

Endo capillary proliferative glomerulonephritis -1

Thrombotic microangiopathy -1

The 19 follow up biopsies, 6 biopsies were categorized as normal (LM and IF) the remaining 13 biopsies which showed abnormalities, 5 had interstitial inflammation characterized by lymphocytic infiltrates involving < 30% of the core, 1 had infiltrates of 30-50%. Interstitial fibrosis involving <30% core was found in 3 patients (26.3%), 30-50% in 2 (15.78%), >50% in 1 (10.52%). Membrano proliferation pattern was found in 1, mesangial proliferation in 1, Glomerulosclerosis involving 50% of glomeruli in one, patchy cortical necrosis in one and hyaline arteriosclerosis in another.

All the patients who were overall normal at discharge were found to by normal at follow up. All the 6 normal biopsies were associated with isolated renal abnormalities, 1 with hematuria alone had mesangial proliferation with IgM C3, mesangial deposits. All the patients who had renal dysfunction had abnormal renal biopsies.


Follow up Renal Biopsy
Normal-6
Abnormal-13
No biopsy-71

Specific renal biopsy breakup:

Biopsy at AKI presentation	Follow up normal Biopsy	Follow up abnormal Biopsy
ATN(n=23)	2	2
AIN(n=7)	2	4
ATN/AIN(n=5)	2	3
TMA with cortical necrosis (n=3)	0	2
Endocapillary proliferation with exudation(n=3)	0	2

In the ATN Group 19 had complete recovery (biopsy not done), 2 had normal biopsies and the remaining two had abnormal biopsies (focal interstitial inflammation, tubular atrophy involving < 30%).

In the AIN group, 4 were abnormal (interstitial inflammation < 30%) -2, 30-50% - 1, interstitial fibrosis 30- 50% in 2 patients, >50% in 1.

In the combined ATN / AIN, 3 had abnormal biopsies with interstitial inflammation with fibrosis involving < 30%.

Endocapillary GN on follow up showed membranoproliferative pattern in 1, another one showed glomerulosclerosis involving > 50% of glomeruli (66.66%).

At 3 months follow up, proteinuria was found in 12 patients (13.3%)

Risk factors analysis for ***Proteinuria at the end of three months follow-up:***

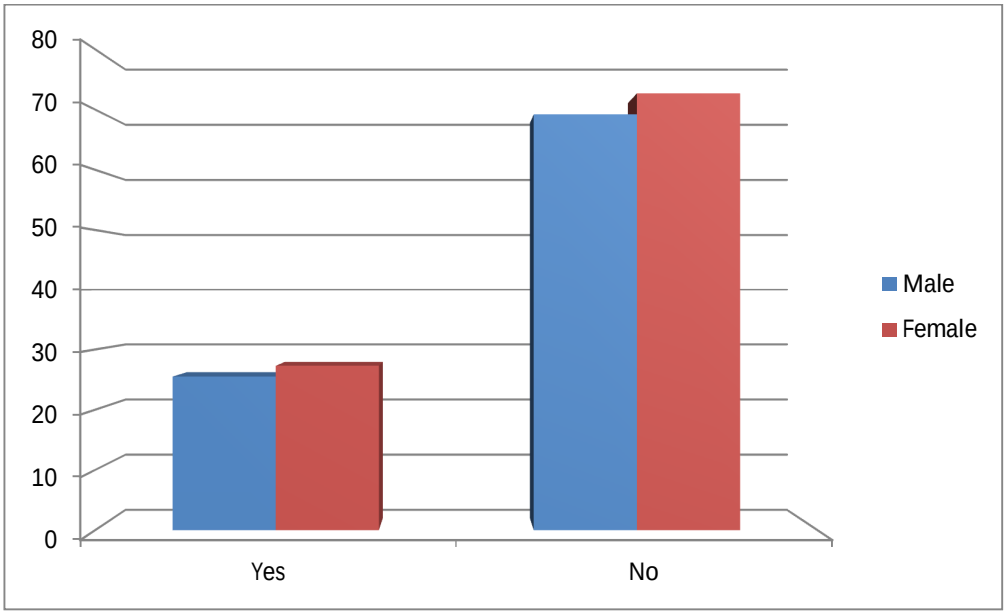
Follow-up proteinuria Vs Sex

Sex	Yes	No	Total	P Value
Male	3(25.5%)	54(69.2%)	57	
Female	9(27.3%)	24(72.7%)	33	0.003
Total	12(13.3%)	78(86.7%)	90	

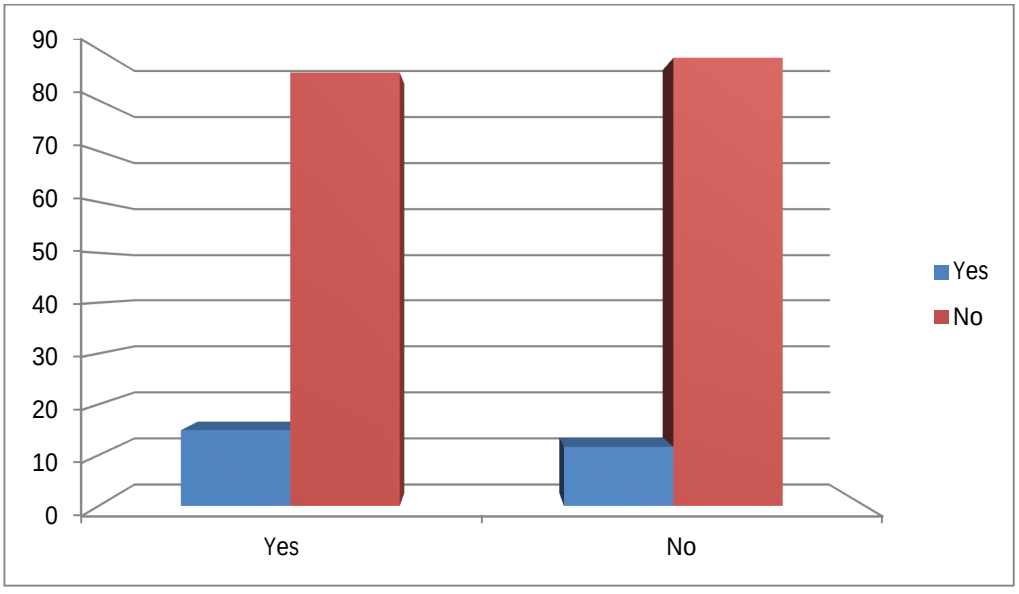
Follow-up proteinuria Vs Presentation Proteinuria

	Yes	No	Total	P Value
Yes	7(14.9%)	40(85.5%)	47	
No	5(11.6%)	38(88.4%)	43	0.649
Total	12(13.3%)	78(86.7%)	90	

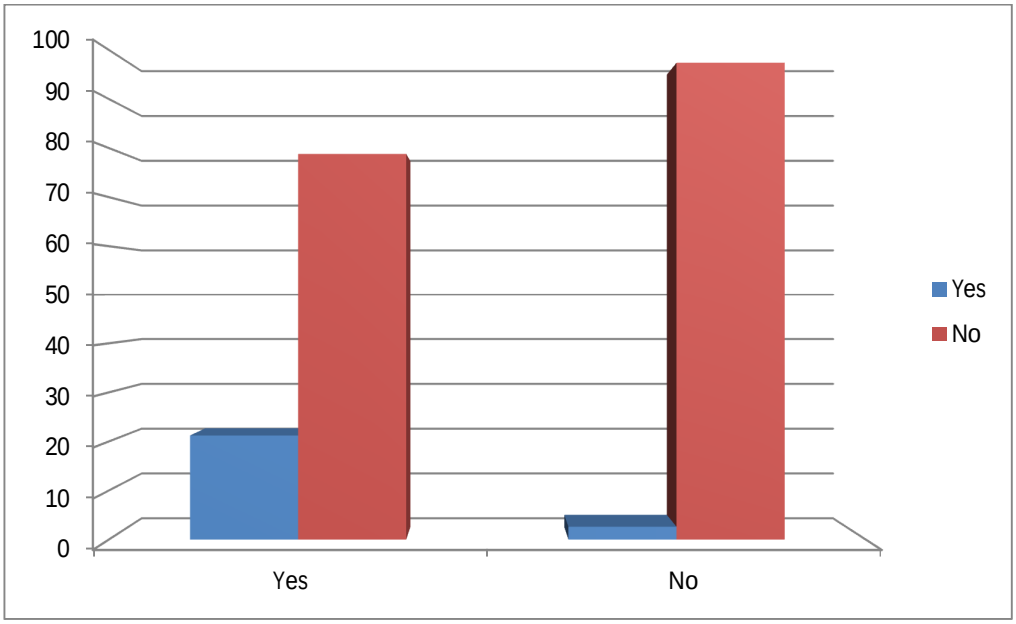
Follow up Proteinuria Vs Sex



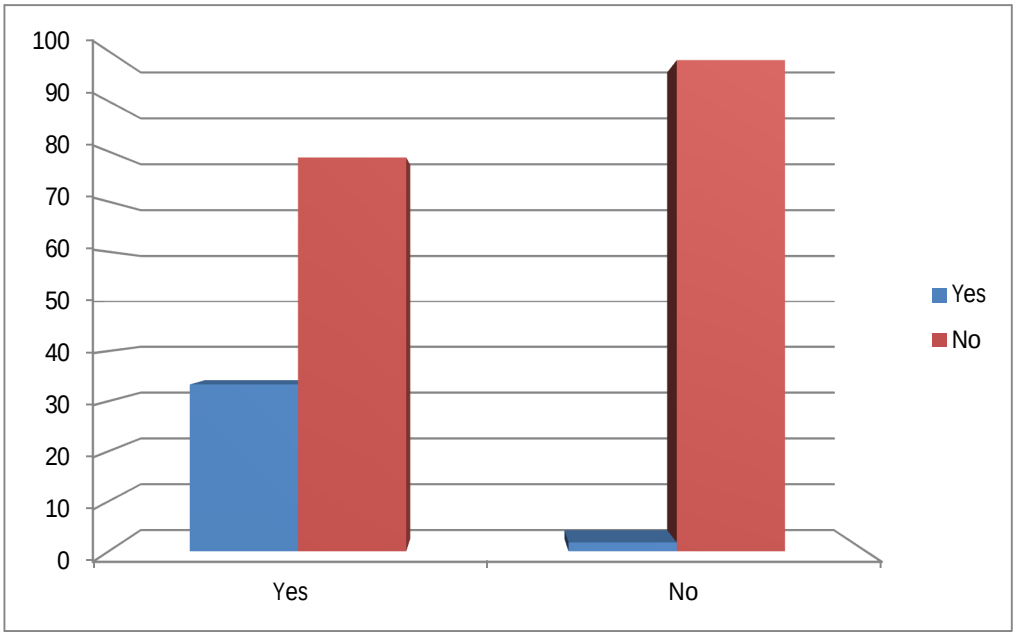
Followup Proteinuria Vs Presentation Proteinuria



Followup Proteinuria Vs Presentation Haematuria



Followup Proteinuria Vs Discharge Urine Abnormalities



Follow-up proteinuria Vs Presentation Haematuria

	Yes	No	Total	P Value
Yes	11(21.2%)	41(78.8%)	52	
No	1(2.6%)	37(97.4%)	38	0.011
Total	12(13.3%)	78(86.7%)	90	

Follow-up proteinuria Vs Presentation Urine Abnormalities

	Yes	No	Total	P Value
Yes	1	22	23	
No	11	56	67	0.114
Total	22	78	90	

Follow-up proteinuria vs Management

	Yes	No	Total	P Value
Conservative	1	29	30	
RRT	11	48	59	0.72
Total	0	1	1	

Follow-up proteinuria Vs Discharge Urine abnormalities

	Yes	No	Total	P Value
Yes	12	35	47	
No	0	43	43	<0.001
Total	12	78	90	

Follow-up proteinuria Vs Discharge GFR

	GFR > 90	**GFR ≤ 90**	**Total**	**P Value**
Yes	34(73.9%)	12(26.1%)	46	
No	37(84.1%)	7(15.9%)	44	0.237
Total	71(78.9%)	19(21.1%)	90	

Comparison of Mean values with *Follow-up proteinuria*:

	Yes	**No**	**P Value**
Age	38.5±14.6	39.1±13.1	0.89
Hemoglobin	9.2±1.41	10.8±2.39	0.027
Presentation Sr. Creatinine	6.117±3.05	5.226±2.94	0.335
Peak Sr. Creatinine	7.5±2.06	7.2±3.3	0.776
Presentation Urea	169.5±90.2	130±61.97	0.058
Peak Urea	194±71.16	156.27±57.3	0.043
Hemodialysis from day of detection	3.18±1.5	3.02±1.9	0.80
Discharge Sr. Creatinine	3.25±1.24	1.99±0.97	0.001

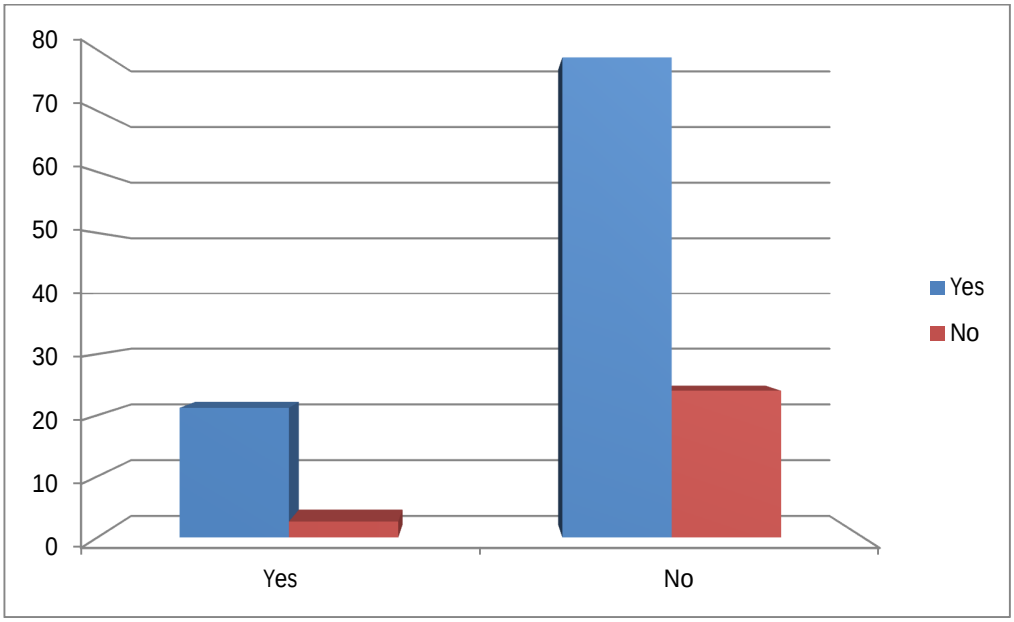
Multiple logistic regression analysis for proteinuria at follow-up:

	Observed		Predicted		
			Proteinuria		Percentage Correct
			Yes	No	
Step 1	Follow up Proteinuria	Yes	9	3	75.0
		No	1	77	98.7
	Overall Percentage				95.6

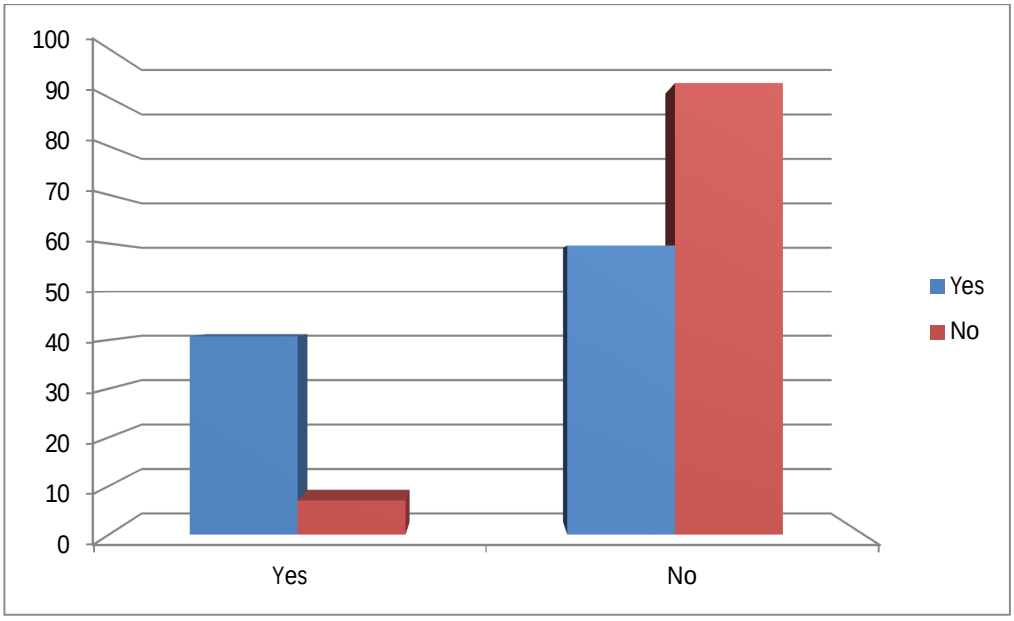
a The cutoff value is .500

	B	S.E.	Wald	df	Sig.	95.0% C.I.for EXP(B)	
						Lower	Upper
AGE	.072	.060	1.456	1	.228	.956	1.209
SEX	.208	1.618	.017	1	.898	.052	29.325
HB	1.038	.695	2.234	1	.135	.724	11.015
PEAK CREATININE	1.765	.808	4.769	1	.029	1.198	28.466
PRESENTATION CREATININE	-.661	.443	2.225	1	.136	.217	1.231
PEAK UREA	-.088	.056	2.467	1	.116	.820	1.022
PRESENTATION UREA	.023	.034	.470	1	.493	.958	1.093
PRESENTATION URINE ABNORMALITIES	3.681	2.394	2.364	1	.124	.364	4326.865
DISCHARGE CREATININE	1.138	1.114	1.043	1	.307	.351	27.721
DISCHARGE UREA	-.128	.064	3.992	1	.046	.775	.998
DISCHARGE URINE ABNORMALITIES	29.467	3388.396	.000	1	.993	.000	.
MANAGEME	.779	2.872	.073	1	.786	.008	606.993

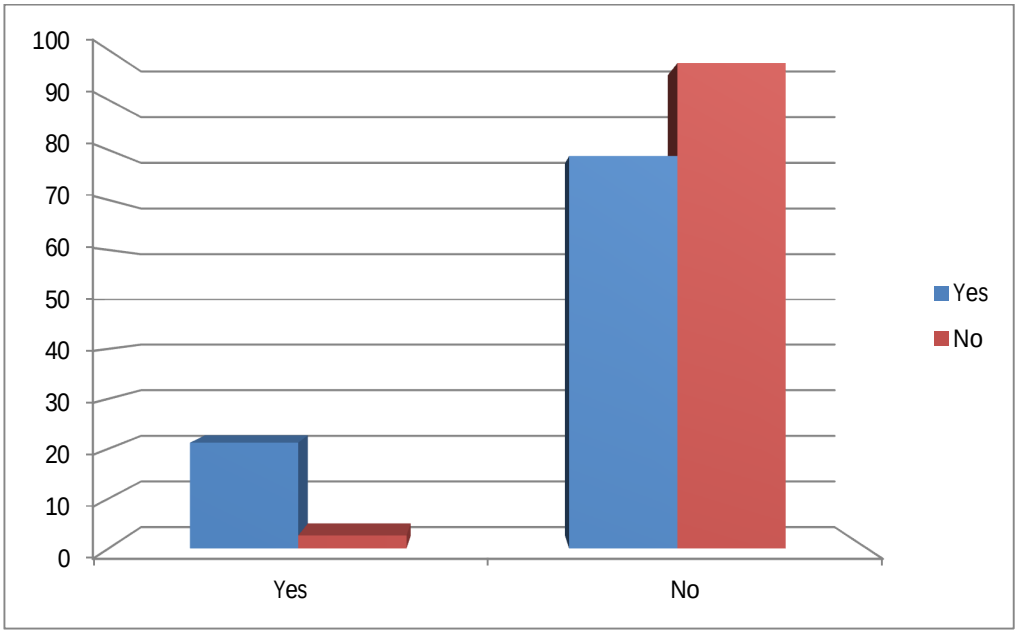
Followup Haematuria Vs Presentation Haematuria



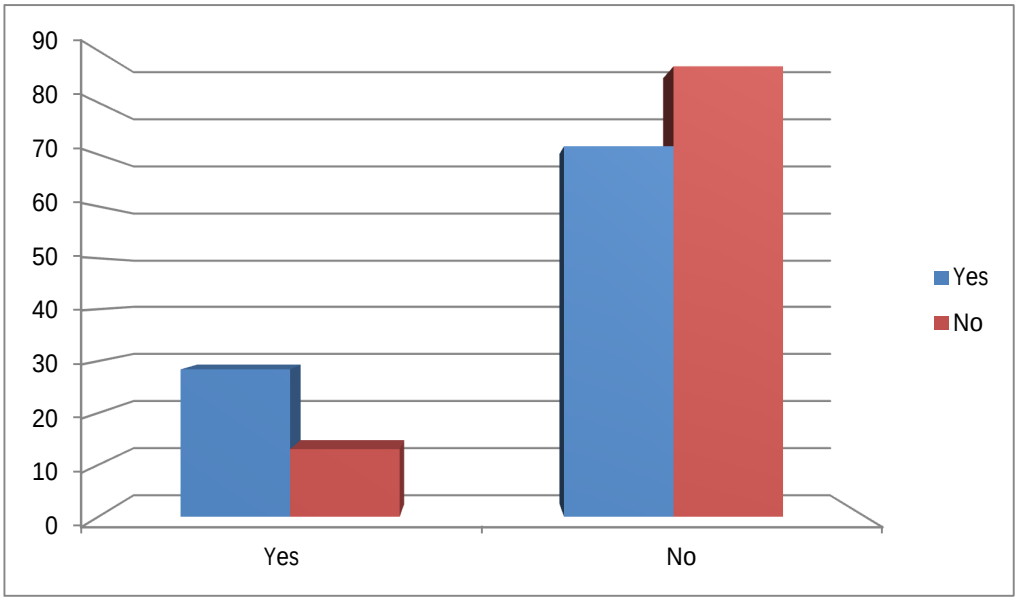
Followup Haematuria Vs Discharge Urine Abnormalities



Followup Haematuria Vs Presentation Haematuria



Followup Haematuria Vs Presentation Urine Abnormalities



Discharge Creatinine and urea were considered to be the risk factors associated with proteinuria at 3 months.

Risk factors analysis for follow up Haematuria:

Follow-up Hematuria Vs Sex

Sex	Yes	No	Total	P Value
Male	15(26.3%)	42(73.7%)	57	
Female	7(21.2%)	26(78.8%)	33	0.587
Total	22(22.4%)	68(78.6%)	90	

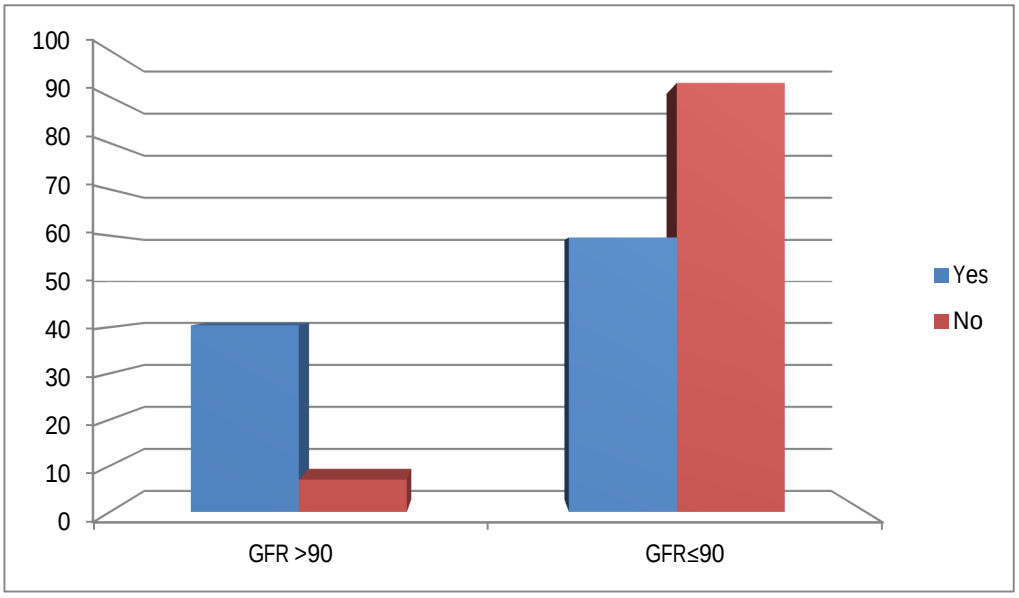
Follow-up Hematuria Vs Presentation Proteinuria

	Yes	No	Total	P Value
Yes	13(27.7%)	34(72.3%)	47	
No	9(20.9%)	34(79.1%)	43	0.458
Total	22(24.4%)	68(75.6%)	90	

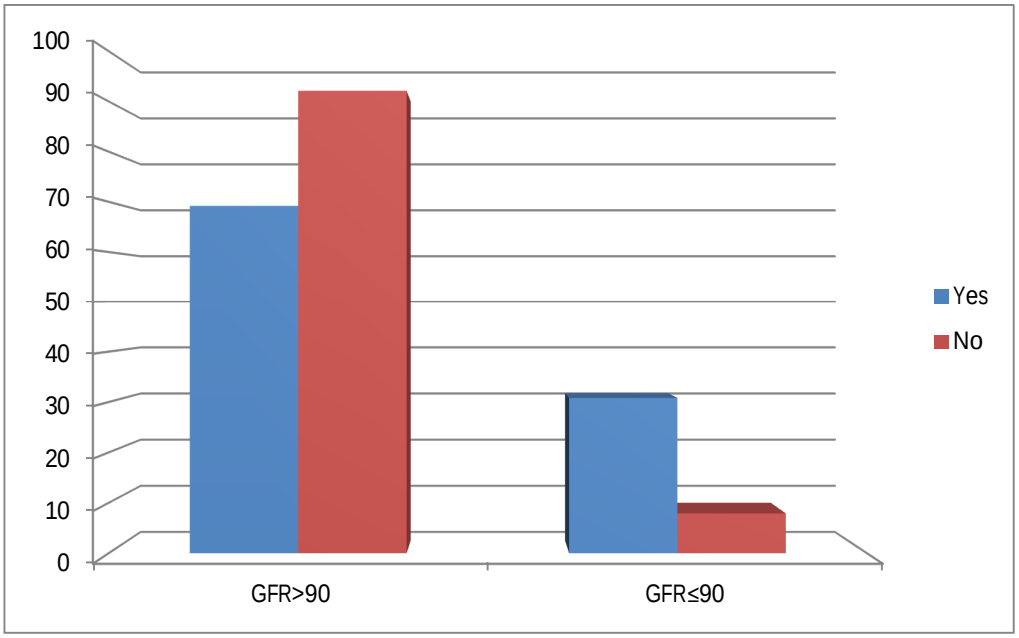
Follow-up Hematuria Vs Presentation Hematuria

	Yes	No	Total	P Value
Yes	11(21.2%)	41(78.8%)	52	
No	1(2.6%)	37(97.4%)	38	0.011
Total	12(13.3%)	78(86.7%)	90	

Followup Haematuria Vs Discharge GFR



Followup Renal Dysfunction Vs Presentation Haematuria



Follow-up Hematuria Vs Presentation Urine Abnormalities

	Yes	No	Total	P Value
Yes	19	48	67	
No	3	20	23	0.114
Total	22	68		

Follow-up Hematuria Vs Management

	Yes	No	Total	P Value
Conservative	3	27	30	
RRT	19	41	60	0.042
Total	22	68	90	

Follow-up Hematuria Vs Discharge Urine abnormalities

	Yes	No	Total	P Value
Yes	19	28	47	
No	3	40	43	0.001
Total	22	68	90	

Follow-up Hematuria Vs Discharge GFR

	GFR > 90	GFR ≤ 90	Total	P Value
Yes	22	48	70	
No	0	20	20	0.002
Total	22	68	90	

Follow-up Hematuria Vs. Anemia

	Yes	No	Total	P Value
Yes	17	43	60	
No	5	25	30	0.225
Total	22	68	90	

Comparisons of Mean values for Hematuria at follow *up*:

	Yes	No	P Value
Age	38.59±13.97	39.16±14.01	0.86
Hemoglobin	9.91±1.9	10.81±2.4	0.118
Presentation Sr. Creatinine	5.159±2.61	5.404±3.07	0.738
Peak Sr. Creatinine	8.8±3.19	6.83±3.02	0.11
Presentation Urea	151.59±74.23	130.26±64.41	0.097
Peak Urea	179.95±58.27	155.26±60.13	0.095
Hemodialysis from day of detection	2.79±1.18	3.17±2.167	0.476
Discharge Sr. Creatinine	3±0.98	1.83±0.985	0.001

***Multiple logistic regression analysis for Hematuria at follow up*:**

		Observed	Predicted		
			Hematuria		Percentage Correct
			Yes	No	
Step 1	Follow up Hematuria	Yes	13	9	59.1
		No	4	64	94.1
	Overall Percentage				85.6

a The cutoff value is .500

	B	S.E.	Wald	df	Sig.	95.0% C.I.for EXP(B)	
						Lower	Upper
AGE	-.030	.029	1.086	1	.297	.918	1.027
SEX	1.686	.903	3.487	1	.062	.920	31.695
HB	.009	.193	.002	1	.962	.691	1.474
PEAK CREATININE	-.121	.224	.294	1	.588	.571	1.373
PRESENTATION CREATININE	.598	.266	5.070	1	.024	1.081	3.061
PEAK UREA	.004	.018	.047	1	.828	.970	1.039
PRESENTATION UREA	-.016	.015	1.229	1	.268	.956	1.013
PRESENTATION URINE ABNORMALITIES	.065	1.056	.004	1	.951	.135	8.454
DISCHARGE CREATININE	-1.020	.574	3.162	1	.075	.117	1.110
DISCHARGE UREA	.002	.020	.007	1	.933	.963	1.042
DISCHARGE URINE ABNORMALITIES	2.800	.969	8.354	1	.004	2.463	109.827
MANAGEME	-.821	1.033	.632	1	.427	.058	3.332

Presentation Sr.creatinine, discharge urinary abnormalities were associated with the risk of hematuria at 3 months.

***Risk factors analysis for follow up renal dysfunction*:**

Follow-up renal Dysfunction Vs Sex

Sex	GFR > 90	GFR ≤ 90	Total	P Value
Male	46(80.7%)	11(19.3%)	57	
Female	25(75.8%)	8(24.2%)	33	0.580
Total	71(78.9%)	19(21.1%)	90	

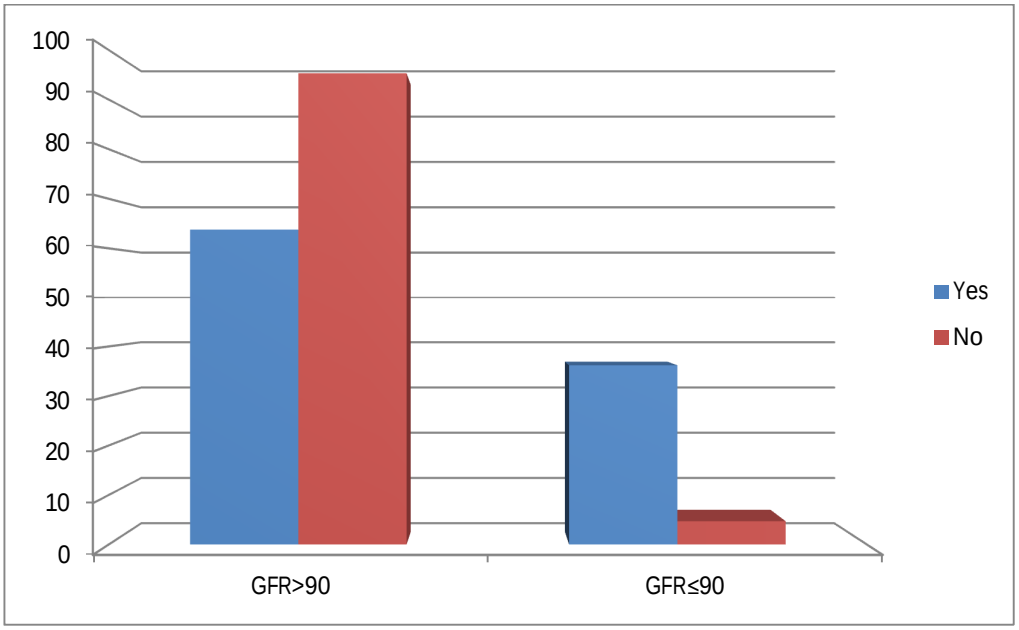
Follow-up Renal Dysfunction Vs Presentation Proteinuria

	GFR > 90	GFR ≤ 90	Total	P Value
Yes	37(78.7%)	10(21.3%)	47	
No	34(79.1%)	9(20.9%)	43	0.968
Total	71(78.9%)	19(21.1%)	90	

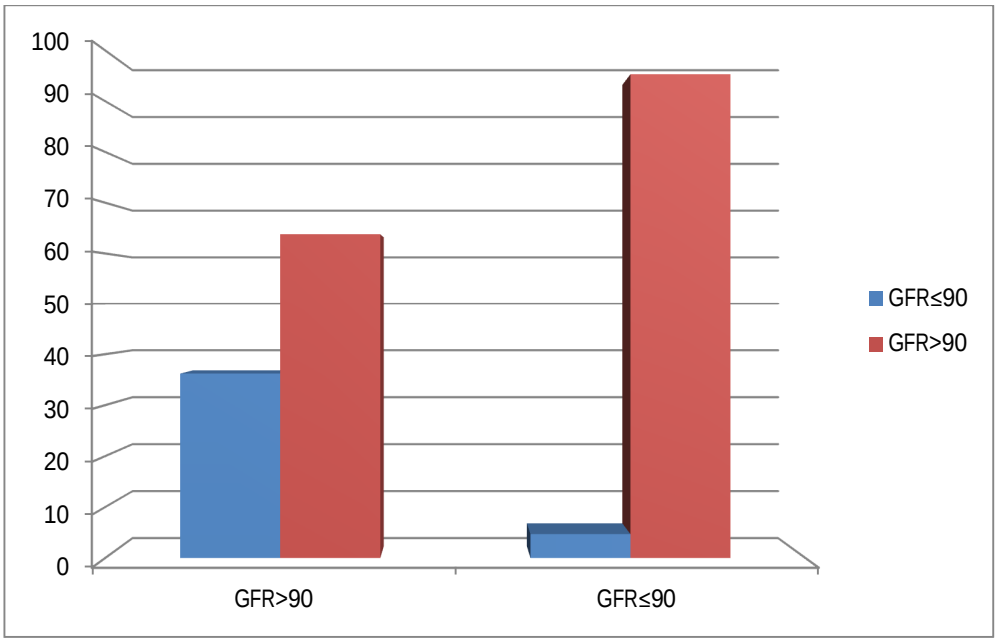
Follow-up Renal Dysfunction Vs Presentation Hematuria

	GFR > 90	GFR ≤ 90	Total	P Value
Yes	36(69.2%)	16(30.8%)	52	
No	35(92.1%)	3(7.9%)	38	0.009
Total	71(78.9%)	19(21.1%)	90	

Followup Renal Dysfunction Vs Management



Followup Renal Dysfunction Vs Discharge GFR



Follow-up Renal Dysfunction Vs Presentation Urine Abnormalities

	GFR > 90	GFR ≤ 90	Total	P Value
Yes	50	17	67	
No	21	2	23	0.076
Total	71	19	90	

Follow-up Renal Dysfunction Vs Management

	GFR > 90	GFR ≤ 90	Total	P Value
Conservative	28	2	30	
RRT	43	17	60	0.031
Total	71	19	90	

Follow-up Renal Dysfunction Vs Discharge Urine abnormalities

	GFR > 90	GFR ≤ 90	Total	P Value
Yes	30	17	47	
No	41	2	43	0.001
Total	71	19	90	

Follow-up Renal Dysfunction Vs Discharge GFR

	GFR > 90	GFR ≤ 90	Total	P Value
GFR > 90	20	0	20	
GFR ≤ 90	51	19	70	0.004
Total	71	19	90	

Comparison of Mean values with *follow up Renal Dysfunction :*

	Yes	No	P Value
Age	38.08±14.21	42.53±12.52	0.219
Hemoglobin	10.81±2.44	9.78±1.72	0.09
Presentation Sr. Creatinine	5.17±3.04	5.98±2.58	0.288
Peak Sr. Creatinine	6.95±3.19	8.66±2.75	0.035
Presentation Urea	129.37±63.98	158.32±75.32	0.095
Peak Urea	154.7±58.95	185.95±60.48	0.044
Hemodialysis from day of detection	3.05±2.13	3.05±1.97	0.98
Discharge Sr. Creatinine	1.78±0.76	3.38±1.25	0.001

Logistic regression analysis for follow up renal dysfunction:

	Observed		Predicted		
			Fol creat		Percentage Correct
			Normal	Abnormal	
Step 1	Follow up creatinine	Normal	68	3	95.8
		Abnormal	7	12	63.2
	Overall Percentage				88.9

The cutoff value is .500

Observed			Predicted		
			Fol creat		Percentage Correct
			Normal	Abnormal	
Step 1	Fol creat	Normal	67	4	94.4
		Abnormal	3	16	84.2
	Overall Percentage				92.2

a The cut-off value is .500

	B	S.E.	Wald	df	Sig.	95.0% C.I.for EXP(B)	
						Lower	Upper
AGE	.079	.046	3.026	1	.082	.990	1.184
SEX	-1.512	1.403	1.161	1	.281	.014	3.451
HB	.496	.335	2.191	1	.139	.852	3.165
PEAK CREATININE	-.304	.272	1.242	1	.265	.433	1.259
PRESENTATION CREATININE	-.206	.341	.365	1	.546	.417	1.589
PEAK UREA	.021	.023	.857	1	.354	.976	1.069
PRESENTATION UREA	-.014	.017	.716	1	.398	.954	1.019
PRESENTATION URINE ABNORMALITIES	2.158	1.684	1.642	1	.200	.319	234.763
DISCHARGE CREATININE	3.445	1.238	7.746	1	.005	2.771	354.874
DISCHARGE UREA	-.051	.032	2.577	1	.108	.892	1.011
DISCHARGE URINE ABNORMALITIES	-4.904	1.781	7.578	1	.006	.000	.244
MANAGEME	2.938	2.018	2.120	1	.145	.362	984.801

Discharge Sr.creatinine & Discharge urinary abnormalities were associated with the renal dysfunction at follow up.

***Risk factors analysis of Overall follow-up abnormalities*:**

Overall follow-up abnormalities vs Sex.

Sex	Normal	Abnormal	Total	P Value
Male	39	18	57	
Female	21	12	33	0.643
Total	60	30	90	

Overall follow-up abnormalities Vs Presentation Proteinuria.

	Normal	Abnormal	Total	P Value
Yes	0	12	12	
No	60	18	78	.001
Total	60	20	92	

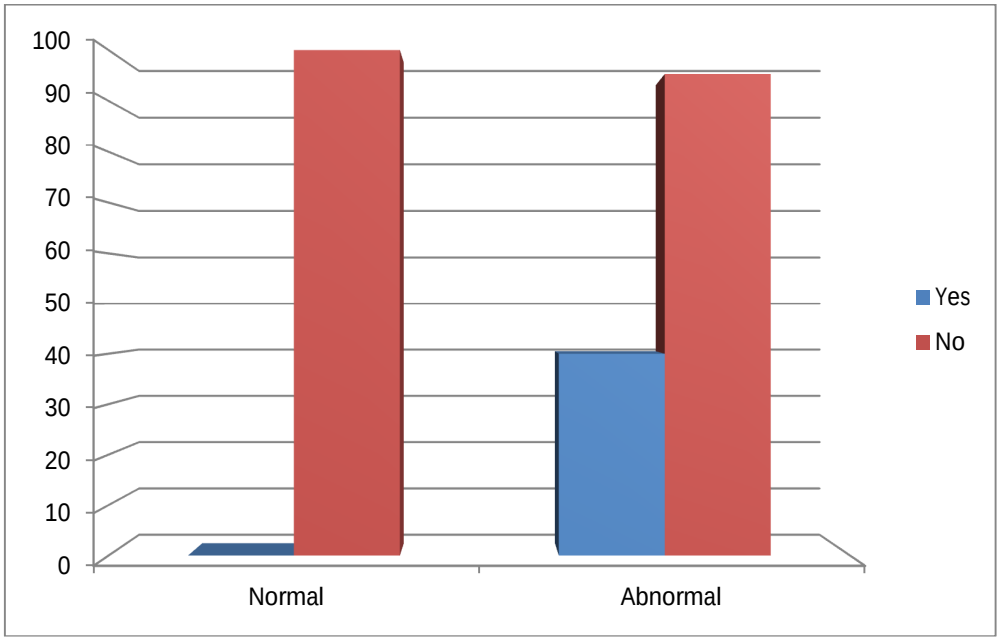
Overall follow-up abnormalities Vs Presentation Haematuria

	Normal	Abnormal	Total	P Value
Yes	0	22	22	
No	60	8	68	0.001
Total	60	30	90	

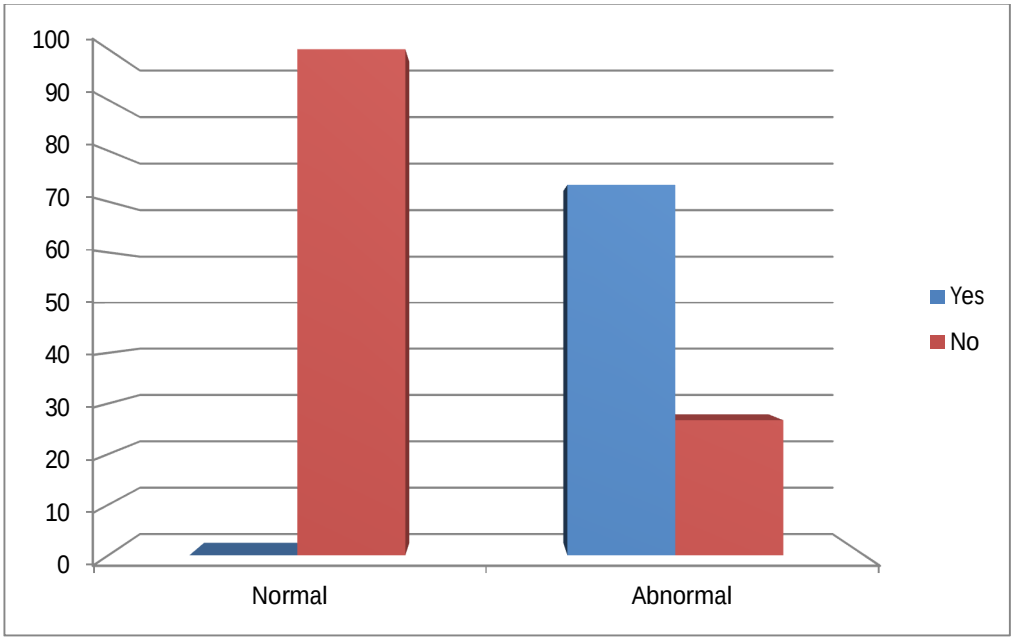
Overall follow-up abnormalities Vs Presentation Urine Abnormalities

	Normal	**Abnormal**	**Total**	**P Value**
Yes	20	3	23	
No	40	27	67	0.013
Total	60	30	90	

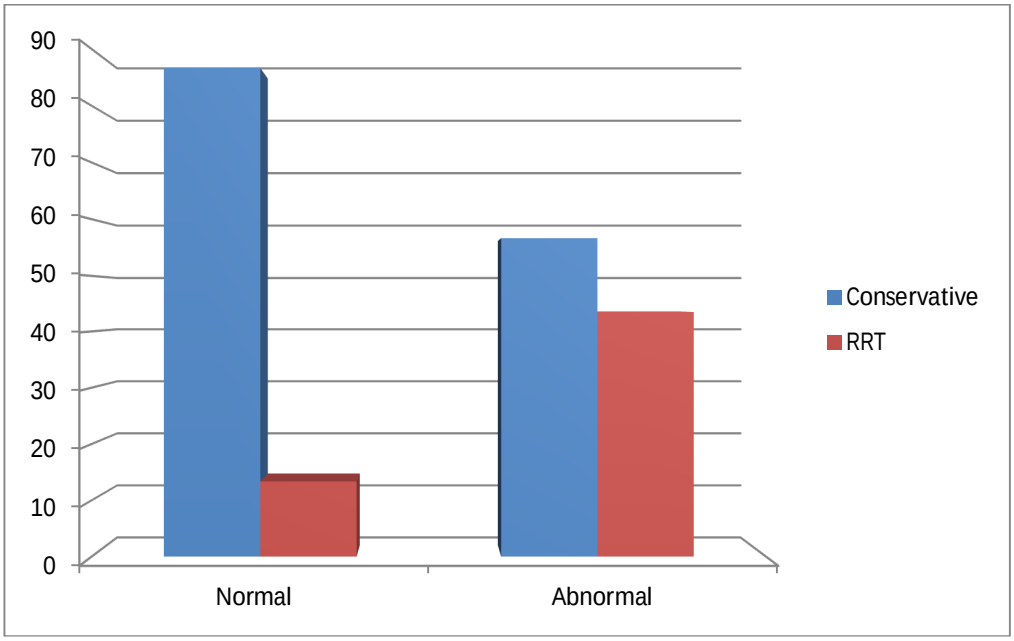
Overall Followup Abnormalities Vs Presentation Proteinuria



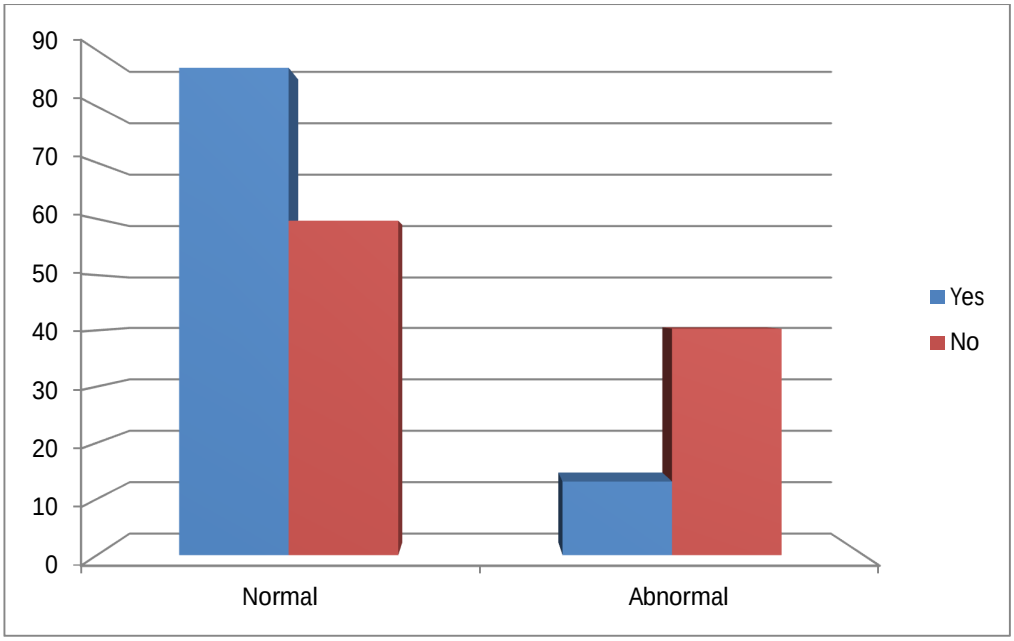
Overall Followup Abnormalities Vs Presentation Haematuria



Overall Followup Abnormalities Vs Management



Overall Followup Abnormalities Vs Presentation Urine Abnormalities



Overall follow-up abnormalities Vs Management

	Normal	Abnormal	Total	P Value
Conservative	26	4	30	
RRT	34	26	60	0.011
Total	60	30	90	

Overall follow-up abnormalities Vs Discharge Urine abnormalities

	Normal	Abnormal	Total	P Value
Yes	39	4	43	
No	21	26	47	0.001
Total	60	30	90	

Overall follow-up abnormalities vs Old Age

	Normal	Abnormal	Total	P Value
Yes	44	19	63	
No	16	11	27	0.329
Total	60	30	90	

Overall follow-up abnormalities Vs. Anemia

	Normal	Abnormal	Total	P Value
Yes	36	24	60	
No	24	6	30	0.058
Total	60	30	90	

Comparison of Mean variables for *overall follow-up abnormalities*:

	Normal	Abnormal	P Value
Age	38.72±14.16	39.63±13.64	0.77
Hemoglobin	10.95±2.54	9.86±1.69	0.037
Presentation Sr. Creatinine	6.618±2.97	8.707±3.2	0.003
Peak Sr. Creatinine	6.95±3.1	8.66±2.7	0.035
Presentation Urea	151.53±59.76	180.83±57.43	0.029
Peak Urea	154.7±58.95	185.95±60.48	0.44
Discharge Sr. Creatinine	1.68±.73	2.98±1.20	0.001

Logistic regression analysis:

	Observed		**Predicted**		
			Fol overa		**Percentage Correct**
			Normal	**Abnormal**	
Step 1	Follow up overall	Normal	57	3	95.0
		Abnormal	7	23	76.7
	Overall Percentage				88.9

a The cutoff value is .500

	B	S.E.	Wald	df	Sig.	95.0% C.I.for EXP(B)	
						Lower	Upper
AGE	.014	.025	.306	1	.580	.966	1.064
SEX	-.527	.789	.446	1	.504	.126	2.771
HB	.103	.198	.270	1	.603	.752	1.633
PEAK CREATININE	-.049	.185	.071	1	.791	.662	1.369
PRESENTATION CREATININE	-.161	.186	.745	1	.388	.591	1.227
PEAK UREA	.004	.015	.085	1	.770	.976	1.034
PRESENTATION UREA	.005	.012	.159	1	.690	.981	1.030
PRESENTATION URINE ABNORMALITIES	1.326	1.187	1.249	1	.264	.368	38.572
DISCHARGE CREATININE	2.009	.665	9.122	1	.003	2.024	27.461
DISCHARGE UREA	-.026	.022	1.468	1	.226	.934	1.016
DISCHARGE URINE ABNORMALITIES	-3.103	.930	11.126	1	.001	.007	.278
MANAGEME	.788	.917	.740	1	.390	.365	13.265

Discharge Sr.creatinine & Discharge urinary abnormalities were associated with the risk of overall follow up abnormalities.

DISCUSSION

DISCUSSION

This study was designed to know the characteristics and short term (3 months) outcome of 96 AKI patients belonging to AKIN stage III. In this study, other co-morbid illnesses like systemic hypertension, Diabetes mellitus, previous renal illness, obstructive uropathy and decompensated liver disease where excluded. This study was intended on adult patients with the median age group in our study is 36 years, representing mainly middle aged population. 30.2% of the patient were in >50 years age group. The maximum age in this study was 66 years. Since this study has more middle aged populations devoid of the above mentioned co morbid illness, it has best characterized the outcome of severe AKI. There was a nearly equal distribution of sex in this study with male: female ratio was 1.6:1. This study included only the intrinsic renal AKI(by FeNa) , since this group best characterize the outcome in contrary to Pre renal and Post renal AKI. The Post renal AKI was excluded in view of difficulty in accessing the duration of AKI and also the pre existing renal abnormalities could not be ruled out.

At presentation, oliguria/ anuria, volume overload and anemia was present in 70.88%, 23.95% and 66.66% respectively. The impact of AKI on anemia could not be studied since most of the patients on

admission were anemic. The peak Serum creatinine and Blood urea were 7.2 mg/dl and 162 mg/dl respectively indicating this study population had severe renal failure and hence the renal outcome could be better studied. Hyperkalemia was noted in 12.5% of the patients. Hyperkalemia in AKI is due to reduced glomerular filtration rate, decreased tubular secretion of potassium, tissue break down and metabolic acidosis (65). Hyponatremia was the commonest abnormality noted with 54.1% of AKI patients developing it .Hyponatremia occurs mainly due to increased fluid retention and less commonly due to sodium depletion (hypovolemia)(65). Urinary abnormalities like Haematuria and/or proteinuria was identified in 70 patients (72.91%) on admission. All the patients had FeNa >2, indicating intrinsic AKI. Haematuria was defined as either dipstick positive or RBC > 2 / hpf in unspun urine, while proteinuria was defined as spot urine PCR >0.3. Only few patients with adequate urine output did have normal urinary microscopy. 68% of the patients underwent renal replacement therapy. Among them only one received acute peritoneal dialysis (PD. PD has always been considered as inferior to hemodialysis in AKI (53) although a study from Brazil showed that its efficiency is as equal to hemodialysis in AKI (54). The lone patients who underwent PD recovered his renal function completely and regained normal renal

function at 3 month follow-up. The most common indications for RRT were volume overload (70%), uremic encephalopathy (20%) and hyperkalemia (18%). None had uremic pericarditis. The mean number of days of HD initiation from the detection of AKI was 3±2.29 days and the mean number of HD sessions was 8±3.14 days. 34.37% received conservative management. The mean age, sex, mean presenting and peak Blood urea, mean presenting and peak Serum creatinine, Serum sodium and potassium & mortality were comparable between the 2 groups. The discharge Serum creatinine were significant between the groups, 2.32± 1.22 mg/dl in RRT group and 1.72±0.68 mg/dl in conservative group (P=0.015).Mean Hemoglobin concentration (p=0.005),presence of Oliguria/anuria(p=0.002),mean presenting Creatinine(0.021),peak blood urea(0.001) vary significantly between the groups. Mortality between two groups could not be compared because all the three deaths in the conservative groups were out of multi organ dysfunction and hypotension that precluded hemodialysis that time. The mortality rate in AKI depends on the cause and the setting of the occurrence of the AKI which varies between 20-70%, with sepsis AKI in critical care units having 70% mortality (67,68,69). The lower mortality rate in our series probably explains the fact that majority of the patients had non critical care illness AKI. Discharge urine abnormalities

were present in 60.83% of RRT group and 30.3% in conservative group (p=0.018). At discharge renal dysfunction, defined as GFR < 90ml/min as per Cockcroft- gault method was found in 77.77%. As per Schiffl et al., 57% of the survivors of critically ill dialysis requiring AKI patients regained normal renal function at discharge and none of the remaining 43% required RRT(70) . In contrary, our series had more patients with renal dysfunction at discharge and 5 patients remained dialysis dependent at discharge. Urinary abnormalities was present in 48.93% of the patients, the mean serum creatinine at the time of discharge was 2.11±1.1 mg/dl. Another study looking at the AKI in critical ill patients found that 4-18% of patients expired after discharge. In this study, only one patient expired during the follow-up period.

The overall discharge abnormalities which included hematuria and/or proteinuria and/or renal dysfunction were found in 87.77%. Acute Tubular Necrosis (ATN) typically follows three phase like initiation phase, maintenance phase, which lasts for 1.2 weeks and recovery phase or diuretic phase. The expected recovery from ATN is usually 3-4 weeks from its insult although conversion to acute cortical necrosis makes the recovery unlikely. Although initial insult in ischemic or nephrotoxic ATN occurs in the tubular epithelial cells, which contributes to the initiation phase, it is the endothelial cell injury that

contributes to the maintenance or oliguric phase. Also, the endothelial injury triggers vasoconstriction, intra vascular coagulation causing decrease in the density of interstitial capillaries termed as vascular dropouts to the range of 30-50%(61). These vascular drop outs result in persistent ischemia to the interstitium which eventually results in interstitial fibrosis and hence progressive chronic kidney disease. AKI can cause ESRD directly, increase the risk of developing CKD and also worsens the underlying CKD. Severity, duration and frequency of AKI, advanced age, presence of Diabetes mellitus, low baseline GFR, low Sr.albumin are considered to be the risk factors in the progression to advanced CKD(71, 72). Our study is unique in the sense that urinary abnormalities along with renal dysfunction were taken into consideration for assessing renal damage. The patients who had either proteinuria or Hematuria or renal dysfunction were subjected for renal biopsy. The overall follow up abnormalities defined as the presence of either Hematuria or proteinuria or renal dysfunction or abnormal renal biopsy was present in 30 patients (33.33%). Renal dysfunction defined as GFR<90ml/min was present in 18 patients (20%).

Isolated urinary abnormalities without renal dysfunction were found in 16.66% of the patients. The follow-up renal biopsy was done in 19 out of 30 patients who fulfilled the criteria of renal biopsy among the

left over 11 patients, 5 had dialysis dependent renal failure and other 2 had severe renal failure (GFR<30ml/min) with echogenic smaller kidneys. Hence biopsy was deferred in these 7 patients. The remaining 4 patients refused for renal biopsy. Among them one had renal dysfunction alone and other three had micro-hematuria alone. The common histological abnormalities found were interstitial inflammation in 6, interstitial fibrosis and tubular atrophy in 6, mesangial proliferation, MPGN pattern in 1 each. All the patients who were overall normal at discharge were found to be overall normal at 3 month follow up. All the 6 normal biopsies were associated with isolated urinary abnormalities. As far as the outcome of various histopathologies at presentation are concerned, ATN had the best recovery with 19 out of 23 recovered completely not warranting renal biopsy and only two had abnormal renal biopsies at follow up. Acute interstitial nephritis (AIN) with or without ATN had comparatively poor prognosis with 7/12 having abnormal biopsy and so as TMA (2/3) and Endocapillary proliferative GN (2/3). As far as AIN is concerned, recent case series showed 64% have full recovery and the remaining 36% have partial and severe renal impairment (73).In this study 58.33% had abnormal renal biopsy at 3 months follow up. Regarding the outcome of ATN, 43% had renal failure at one year follow up as per Schiffl et al (74).In this study;

only 9% were found to have renal damage at follow-up. The risk factor analysis showed female sex (p=0.003), lower hemoglobin (p=0.002), presentation Hematuria (p=0.011), discharge urine abnormalities (p=0.001), peak blood urea (p=0.043) and discharge serum creatinine (p=0.001) were significantly associated with proteinuria at 3months follow up. Multi-variate analysis showed discharge serum creatinine and urea were associated with the risk of proteinuria at 3 months. Risk factor analysis of Hematuria at follow up showed presentation Hematuria (p=0.011) RRT requiring (p=0.042), discharge urine abnormalities (p=0.001), discharge GFR (p=0.002) and serum creatinine (p=0.001) were significantly associated with this abnormalities. Multi-variate analysis showed presentation serum creatinine, discharge urinary abnormalities were associated with the risk of Haematuria at 3 months. Presentation Haematuria (p=0.009) , RRT requiring (p=0.031), discharge urine abnormalities (p=0.001), discharge serum creatinine (p=0.001) and peak serum creatinine (p=0.0035) were associated with renal dysfunction at 3 months. Discharge serum creatinine and discharge urinary abnormalities were significantly associated with the risk of renal dysfunction at 3 months. As far as the overall abnormalities at follow up were concerned, this study showed presentation proteinuria (p=0.001), Hematuria (p=0.001), presentation urine abnormalities (p=0.013),

discharge urine abnormalities (p=0.001), presentation serum creatinine (p=0.003), presentation urea (p=0.029), peak serum creatinine (p=0.003) and discharge serum creatinine (p=0.001) were significantly associated with that abnormality at 3 months .Multivariate analysis showed serum creatinine and urinary abnormalities at discharge were associated with the increased risk of overall renal abnormalities at 3 months. Many studies including a study by Ishani et al showed magnitude of Serum creatinine during the post operative period was linked with the progression to CKD among the AKI survivors(75).This study showed presentation, peak and discharge Serum creatinine were associated with risk of renal damage at short term follow up.

CONCLUSIONS

1. Severe AKI (AKIN STAGE III) is common in the hospital setting.

2. The patients who receive RRT have significantly high risk of having high Serum creatinine at discharge, persistent hematuria and renal dysfunction at 3 months.

3. More than two thirds of AKIN III AKI patients have evidence of renal damage at discharge viz., proteinuria, hematuria and renal dysfunction at discharge.

4. Nearly one third of the survivors of severe AKI have evidence of residual renal involvement at 3 months.

5. The patients who have no evidence of residual renal involvement at discharge continue to be the same at 3 months.

6. The patients who are dialysis dependent at discharge continued to be dialysis dependent and vice versa.

7. All the patients who had persistent renal dysfunction have abnormal renal biopsy at 3 months.

8. Acute tubular necrosis (ATN) has the best prognosis among all the AKI histologies. Acute interstitial nephritis in isolation or in combination with ATN has worse prognosis causing persistent interstitial inflammation, fibrosis and tubular atrophy.

9. Discharge urinary abnormalities, Presentation & Discharge Sr. Creatinine are associated with persistent renal involvement at 3 months.

ABBREVATION

TGF – Transforming Growth Factor

IFN-γ – Interferon γ

GLDH – Glutamide Lactate Dehydrogenase

GOD-PAP – Glucose Oxidase Dehydrogenase, Glucose Peroxidase Dehydrogenase

IFCC – International Federation of Clinical Chemistry

BCG – Bromo Cresol Green

TNF – Tumor Necrosis Factor

IL – Inter Leukin

VEGF – Vascular Endothelial Growth Factor

MCP – Membrane Cofactor Protein

AKIN – Acute Kidney Injury Network

KIM – Kidney Injury Molecule

NGAL – Neutrophil Gelatinase Associated Lipocalin

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ANNEXURES

PROFORMA

N.c no:

Name: **Age/Sex:** **IP.No:**

Address: **Ph.No:**

Occupation:

D.O.A: **D.O.D:**

Clinical History/ Finding:

Volume Overload: (JVP// Pedal Edema// Lungs Sings)

Fever: **Drugs:**

Hematuria:

ADD: **Native medicines:**

Encephalopathy:

Jaundice: **DCLD**

Pericarditis:

Snake bite/ **Obstretic:**

Rashes:

Insect sting

Post operative: **Radio Contrast:**

Arthritis:

Hypotension: **Hypertension:**

Others:

Cardiac dysfucntion: **Oliguria:**

Date									
Hb									
TC									
DC									
Platelets									

RBS									
Bld.Urea									
Sr.Creatinine									
Sr.Sodium									
Sr..Potassium									
Sr.Calcium									
Sr.Phosphorus									
Sr.Uric acid									
Sr.bilurubin									
Sr.SGOT									
Sr.SGPT									
Sr.Alk Phos									
Urine Routine									
24 Hr Protein									
FeNA									
Viral Markers									
C3 C4									
ANA									
ASO									
ANCA									
MSAT(Lepto)									
MP									
Cultures Study									
Other Studies									
Urine Output									

USG Abdomen:

X- ray KUB:

X-ray Chest:

Renal Biopsy :

ECG:

Diagnosis :

Management: Conservative// Hemodialysis//Peritoneal Dialysis

Day from detection of ARF:

No. of HD// Cycles Of PD:

Outcome:

Alive/ Death

<u>On Discharge:</u>

Urea **Creatinine** **Urine Routine**

<u>Follow-Up (3 Months)</u>

Urea **Creatinine** **24 Hr Urine Protein**

Urine Routine:

S. No	Name	Age	Sex	RF / Cause	Anuria / Oliguria	Volume overloaded	Other Features	Hb	Highest creatinine	Presentation Creatinine	Highest Urea	Presentation Urea	PresentationNa+	Presentation K+	Proteinuria	Haematuria	Renal Biopsy	Management	HD from dectection of AKI	No. of HD	Discharge Creatinine	Discharge Urea	Urine Protien	Haematuria	Follow up (3 months)					Death	
																									Sr. Creatinine	Urea	Proteinuria	hematuria	Renal Biopsy	Hospital	Follow up
1	Renuga	22	F	Heavy metal investigation	Yes	Yes	-	8.1	14.5	14.5	182	182	134	5.86	Yes	Yes	ATN	H	2	5	2	62	Yes	Yes	1.2	37	Nil	Nil	-	No	No
2	Sekar	52	M	NSAIDS / LVD / fever	No	No	-	11.9	6.3	6.3	143	143	133	4.3	No	Yes	-	C	-	-	3.2	90	No	Yes	1.4	35	Nil	yes	-	No	No
3	Abilash	23	M	Fever / ADD	Yes	Yes	-	10.8	11.1	11.1	207	207	134.9	3.94	No	Yes	ATN	H	7	3	1.5	48	No	yes	1	20	Nil	Nil	-	No	No
4	Parimala	14	F	ADD	Yes	No	E, HO	12.5	8.5	2.8	188	42	129	3.89	Yes	No	-	H	4	8	1.3	45	No	No	1	19	Neg	No	-	No	No
5	Amudha	49	F	Sepsis	No	Yes	-	9.7	10	8.5	171	165	143	4.86	Yes	Yes	ATN	H	2	5	1.8	38	No	Yes	0.9	25	Nil	Nil	-	No	No
6	Rani	60	F	NSAIDS	No	No	HN	10.3	4	3.2	80	78	137	6.7	No	No	-	C	-	-	1	42	Yes	No	1	32	Nil	Nil	-	No	No
7	Ravi	49	M	Malaria	Yes	Yes	E,HN	13.5	9	9	231	231	143	5.37	No	No	-	H	2	14	5	130	No	No	2.7	50	No	yes	CIN	No	No
8	packson	36	M	ADD	Yes	No	-	14.3	5.6	5.6	130	130	139	4.2	No	No	-	C	-	-	2.4	70	No	No	0.9	26	No	No	-	No	No
9	Kovendhan	26	M	Sepsis	Yes	Yes	-	9.7	13.8	3	170	60	139	4.6	Yes	Yes	ATI	H	3	22	2.6	73	Yes	Yes	1.4	50	Nil	yes	-	No	No
10	Murugan	33	M	ADD	Yes	No	-	15.5	3.6	3.6	78	78	135	2.5	No	No	-	C	-	-	1.4	69	Yes	Yes	1	32	Nil	Nil	-	No	No
11	Selva Kumar	58	M	Fever	Yes	Yes	-	10.2	6.9	6.9	150	150	123	5.5	No	No	-	H	7	2	1	20	No	No	1	22	No	No	-	No	No
12	Raji	35	M	ADD	No	No	-	14	10.9	3.2	192	131	123	4.1	Yes	Yes	-	C	-	-	2.7	48	No	No	1	36	No	No	-	No	No
13	Ramu	20	M	Cellulitis/ sepsis	Yes	No	-	10.6	5.8	5.8	168	168	116	2.46	Yes	No	-	C	-	-	1.5	38	No	No	1	22	No	No	-	No	No
14	Govindammal	60	F	ADD	No	No	-	11.2	4.4	1.7	98	58	125	2.7	No	Yes	-	C	-	-	2.8	68	No	No	1	28	Nil	Nil	-	No	No
15	Manimegalai	52	F	ADD	No	Yes	-	9.6	10.1	10.1	252	252	130	4.5	No	Yes	AIN	H	5	4	3.6	100	yes	Yes	1	30	Yes	Nil	Y	No	No
16	Gandhi	44	M	Malaria	No	No	-	8.9	4.6	4.6	110	100	138.6	4.67	Neg	Yes	-	C	-	-	2	40	No	No	1	28	Neg	Nil	-	No	No
17	Rajeswari	66	F	ADD	Yes	Yes	-	7.7	8.5	4	166	68	137	2.1	Yes	Yes	-	H	4	8	1.7	52	No	Yes	0.9	30	Neg	Neg	-	No	No
18	Murugan	33	M	ADD	Yes	-	-	15.5	3.6	3.6	78	78	135	2.5	No	No	-	C	-	-	1.4	69	No	No	1	28	No	No	-	No	No
19	Kovendhan	26	M	Fever	Yes	Yes		9.7	13.6	3	170	170	137	3.8	Yes	Yes	ATN	H	3	22	2.6	73	Yes	Yes	1.4	50	No	Yes	-	No	No
20	Sathish	19	M	sepsis	Yes	Yes	-	10.3	7.3	6.3	167	167	121	3.9	No	Yes	-	H	2	4	1.2	47	Yes	Yes	1	29	Nil	Nil	-	No	No
21	Esther	50	F	NSAIDS	Yes	Yes	-	9.1	8.7	7.1	301	301	118	5.5	No	Yes	AIN	H	5	4	3.9	100	Yes	Yes	3.4	100	Yes	Yes	Chronic interstitial Nephritis, Internal	No	No
22	Joyaraj	25	M	Malaria	Yes	Yes	E, HY, J	7.9	11.9	5	209	195	133	3.7	Yes	Yes	AIN / ATN	H	2	15	3	88	Yes	Yes	1.1	30	No	Yes	Normal	No	No
23	Santhanam	54	M	ADD	No	No		10.8	9.8	9	226	173	133	5.5	Yes	No	-	H	4	5	2.4	35	No	No	1	28	No	No	-	No	No
24	Arumugam	40	M	Pancreatitis	Yes	No	J	7.3	10.1	10.1	359	359	116	3.42	Yes	No	-	C	-	-	2	69	No	No	1	30	No	No	-	No	No
25	Anand	49	M	Leptospirosis	Yes	Yes	HY	7.8	5	4.5	139	121	138	4	Yes	Yes	-	H	2	5	1.8	48	Yes	Yes	1.2	32	No	No	-	No	No
26	Ponnuswamy	40	M	sepsis	Yes	No	-	11.4	11.7	6.4	182	140	137	4.4	Yes	No	-	H	2	3	1.2	40	No	Yes	1	30	No	No	-	No	No
27	Saranya	22	F	post partum	Yes	Yes	J	6.5	6.2	4	126	88	137	3.13	Yes	Yes	TMA, Patcly cortical Necrosis	H	2	9.8	4	98	Yes	Yes	5	100	Yes	Yes	CKD	No	No
28	Sundharamoorthy	35	M	ADD	No	No	-	11	5.2	5.2	212	212	138	3.8	Yes	No	-	C	-	-	1.3	32	No	No	1	28	No	No	-	No	No
29	Shankar	40	M	Sepsis	Yes	No	-	9.9	2.7	2.6	141	132	135	3.6	No	No	-	H	1	1	-	-	-	-	-	-	-	-	-	-	-
30	Kamalakannan	52	M	Sepsis /cardiac failure	Yes	Yes	-	8.2	6.1	2.2	146	71	127	3	No	Yes	-	H	2	4	3.5	145	No	No	0.9	29	No	No	-	-	-
31	Kumar	23	M	NSAIDS	No	No	HY	12.3	4.5	4.5	176	128	128	3.3	Yes	Yes	ATN	H	2	3	1.1	28	Nil	No	1	28	No	No	-	No	-
32	Perumal	48	M	Multiple myeloma	No	No	-	8.5	10.8	10.8	186	186	128.4	6.99	Yes	Yes	Cast Nephropathy , ATN	H	3	10	4.8	116	Yes	Yes	8.4	123	Yes	Yes	interstitial fibrosis / tubular atrophy	No	No
33	Arumugam	55	M	pyelonephritis	Yes	Yes		8.9	7.5	5.9	158	136	116	3.5	Yes	No	-	H	6	3	2.9	49	Nil	Nil	1	30	No	No	-	No	No
34	Karunakaran	53	M	sepsis	Yes	No	E	9	4.8	4.8	262	262	124	7.4	No	No	-	H	1	1	-	-	-	-	-	-	-	-	-	Death	-
35	Nagarathinam	36	M	acute pancreatitis	Yes	Yes	J	17.5	4.8	4.1	188	125	130	5.2	No	No	-	H	3	7	1.9	60	Nil	No	1	29	No	No	-	-	-
36	Ravi	52	M	PIGN	No	No	-	13.5	4.1	3.6	86	86	136	4.5	Yes	Yes	endo capillary proliferation	C	-	-	2.4	80	Yes	Yes	1	30	No	Yes	mesangial proliferation, no interstitial inflammation	-	-
37	Jeyanthi	36	F	Post operative/ sepsis	No	Yes	-	9.4	4.7	4.7	102	102	133	3.25	Yes	Yes	ATN	H	1	3	1	28	No	No	1	28	No	No		-	-
38	Hussain	26	M	fever	No	No	HY	10	5.3	5.3	130	130	138	3.6	Yes	Yes	ATN	C	-	-	1.1	30	Yes	Yes	1	29	Yes	No	Normal	-	-
39	Vasanthi	40	F	sepsis	Yes	No	HO, E	9.8	4.4	2.7	110	120	138	4	No	No	-	C	-	-	-	-	-	-	-	-	-	-	-	Death	-
40	Prakash gosh	35	M	ADD	Yes	No	E	10.4	4.8	4.8	102	102	137	4	No	No	ATN	H	2	5	5.2	120	No	No	-	-	-	-	-	-	No Follow up
41	Pattammal	50	F	ADD	Yes	No		10	3.7	2.4	116	116	145	2.34	No	No	-	C	-	-	1.3	40	No	No	1	27	No	No	-	-	-
42	Krishnan	45	M	ADD	Yes	No	HO	17.4	3.1	3.1	160	160	136	4.9	No	No	-	C	-	-	2.3	72	No	No	1	28	No	No	-	-	-
43	Rajesh	17	M	ADD	No	No	#VALUE!	11.6	10.7	2.7	178	96	131	2.6	Yes	No	ATN	H	7	2	1.6	40	No	No	0.9	30	No	No	-	-	-
44	Krishnan	60	M	Leptospirosis	Yes	No	HY	10.4	8.7	8.5	178	127	122	4.4	Yes	No	ATI/ATN	H	2	4	1.4	34	Yes	No	1.3	40	No	No	tubulo interstial inflamation focal fibrosis	-	-
45	Sathish kumar	23	M	Pancreatitis	Yes	No	E, HY	10.6	4.6	1.5	110	37	130	3.9	No	No	ATN	H	2	2	1.4	36	No	Yes	1.2	38	Yes	Yes	Normal	-	-
46	Gunasundari	22	F	post partum/ sepsis	Yes	Yes	HO	15.1	5.9	3.4	104	95	136	3.3	Yes	No	ATN	H	2	9	1.3	32	No	No	1	30	No	No	-	-	-
47	Zabana	30	F	post operative/ sepsis	Yes	Yes	HY	10.1	4.7	7.2	140	94	134.1	3.07	Yes	Yes	ATN	C	-	-	1.5	25	Yes	Yes	0.9	28	No	No	-	-	-
48	Radha	46	F	cardiac failure	Yes	Yes	HO	12.1	2.6	2.6	96	96	136	4	No	No	-	C	-	-	-	-	-	-	-	-	-	-	-	Death	-
49	Ramesh Kumar	35	M	Leptospirosis	Yes	Yes	E, H, J	10.2	7	6	190	148	140	3.8	Yes	Yes	ATN	PD	11	60 cycles	1.5	40	No	No	1	26	No	No	-	-	-
50	Senthil	30	M	Leptospirosis	Yes	Yes	-	11	7.6	7.6	142	142	137	4.2	No	No	ATN	H	1	5	2.8	57	No	No	1	28	No	No	-	-	-
51	Poovarasan	34	M	ADD / Cocaine	No	Yes	HY, E	9.4	15.6	15.6	285	285	139	4.2	No	No	-	H	1	3	1.4	30	No	No	0.9	30	No	No	-	-	-
52	Ellappan	25	M	acute pancreatitis	No	No	J	11.2	3.5	3.5	113	94	134	3.5	No	No	-	C	-	-	1.2	53	No	No	1	28	No	No	-	-	-
53	Jeyanthi	36	F	sepsis	Yes	Yes	-	9.4	4.7	4.7	102	102	133	3.25	Yes	No	ATN	H	3	3	1	35	No	Yes	1	30	No	No	-	-	-
54	Saraswathy	57	F	sepsis	Yes	Yes	E	9	7.2	1.1	180	41	132	4.3	No	Yes	-	C	-	-	1.7	40	No	No	1	28	No	No	-	-	-
55	Rani	60	F	NSAIDS	No	No	-	10.3	2.1	2.1	45	45	137	3.3	No	2+	-	C	-	-	1	38	No	No	1	29	No	No	-	-	-
56	Vijayalakshmi	19	F	Post patrum	Yes	Yes	-	6.8	4	1.1	60	60	133	3.4	No	No	ATN	H	2	3	1.2	28	No	No	1.1	30	No	No	-	-	-
57	Ravi	52	M	fever	No	No		13.5	4.1	3.6	86	86	137.8	3.92	Yes	Yes	-	C	-	-	1	30	No	No	1	34	No	No	-	-	-
58	Hussain	26	M	fever	No	No	-	13	9.3	5.3	88	50	142	3.2	No	No	-	C	-	-	1	38	No	No	1	30	No	No	-	-	-
59	Dalim	32	M	Post operative/ sepsis	Yes	Yes	E	10.4	7.9	4.5	148	99	130	3.5	Yes	No	-	H	2	8	2.4	82	Yes	Yes	1	34	No	No	-	-	-

60	Ganesan	52	M	fever	Yes	-	-	8.7	4	4	171	118	123.4	3.24	No	No	-	C	-	-	1.3	28	No	No	0.9	30	No	No	-	-	-
61	Sathish kumar	25	M	ADD	Yes	Yes	-	15	6.2	2.9	187	56	127	3.5	No	Yes	ATN	H	4	2	1.2	28	No	No	1	29	No	No	-	-	-
62	Shiva	37	F	PIGN	Yes	Yes	HY	10.6	6.1	6.4	124	124	138.4	5	Yes	Yes	endo capillary proliferation with exudation	H	3	6	4.5	140	Yes	Yes	6.1	140	Yes	-	MPGN	No	No
63	Jeyalakshmi	16	F	PIGN	Yes	No	HY	12.4	3.4	2.5	120	110	136	4	Yes	Yes	exudative proliferation, GN	C	-	-	1.2	30	Yes	Yes	1	40	No	-	-	-	-
64	Khatum Bee	58	F	NSAIDS/ fever	Yes	Yes	E	10	6.4	5.8	130	124	126	3.8	Yes	Yes	ATN	H	1	4	1.4	40	No	No	1.1	36	No	No	-	No	No
65	Nagavalli	54	F	fever	Yes	Yes	HY	12	4.7	1.6	120	100	130	3.9	Yes	Yes	ATN / AIN	H	2	3	1.4	38	No	No	1	34	No	Yes	focal interstitial infiltrates	-	-
66	Sheriff	45	M	acute pancreatitis	Yes	No	-	11	4.5	3	110	104	135	3.8	Yes	Yes	AIN	H	2	4	1.3	40	No	No	1.4	36	No	No	-	No	No
67	Kumar	35	M	acute pancreatitis	Yes	Yes	-	10.6	6.7	5.2	112	102	130	3.4	No	Yes	AIN	H	3	6	2.2	48	No	Yes	1.2	28	no	Yes	Normal	No	No
68	Jeyakumar	36	M	obstructive uropathy/b/l ureteric calculi	Yes	Yes	HY	13.4	8.2	6	140	110	140	3.9	No	Yes	-	H	2	3	1.4	38	No	Yes	1.1	30	No	No	-	-	-
69	Rajesh	28	M	acute pancreatitis	Yes	Yes	-	9.2	8	3.4	222	104	144	4.8	No	Yes	ATN/AIN	H	2	2	-	-	-	-	-	-	-	-	-	Death	-
70	Savithri	50	F	ADD	No	No	-	10.4	3.4	2.6	140	100	128	4	No	No	-	C	-	-	1	28	No	Nil	0.9	38	No	No	-	-	-
71	Zahidha	48	F	AGN/ANCA Vasculitis	Yes	Yes	HY	8.6	8.8	3.4	240	122	134	3.8	Yes	Yes	crescontic GN	H	3	14	6	80	Yes	Yes	-	-	-	-	-	-	death
72	Sivagami	60	F	AGN/ANCA Vasculitis	Yes	Yes	HY	10.4	7.4	4.6	220	184	140	4	Yes	Yes	crescontic GN	H	2	8	-	74	Yes	Yes	1.8	40	Yes	Yes	-	-	-
73	Thavamani	58	F	AGN/PIGN	Yes	Yes	-	9.8	8.4	4.2	210	100	144	5.6	Yes	Yes	crescontic GN	H	2	10	-	-	-	yes	-	-	-	-	-	Death	-
74	Mariappan	16	M	Leptospirosis	Yes	Yes	HY	8.4	4.4	3.2	112	90	148	4.9	Yes	Yes	-	C	-	-	-	-	-	-	-	-	-	-	-	Death	-
75	Lakshmi	22	F	Post partum/ sepsis	Yes	Yes	-	10	6.5	2.4	200	100	131	3.8	Yes	Yes	patchy acute cortical necrosis	H	1	16	2.4	86	Yes	Yes	1.2	40	Yes	Yes		-	-
76	Rekha	22	F	Post partum/ sepsis	Yes	Yes	-	8.1	14	14	180	180	134	5.86	Yes	Yes	ATN	H	2	5	2	70	Yes	Yes	1.2	36	No	No	Interstitial fibrosis, patchy cortical necrosis	-	-
77	Shankar	52	M	ADD	No	No	-	11.9	6.3	6.3	142	142	133	4.3	No	Yes	-	C	-	-	3.2	86	No	Yes	1.4	30	No	2+	-	-	-
78	Parveen	15	F	sepsis	Yes	No	E,HO	12.5	8.5	2.8	207	207	134.9	3.94	No	Yes	ATN	H	7	3	1.4	72	No	yes	1	20	No	No	-	-	-
79	Aruna	49	F	fever	No	Yes	-	9.7	10	8.5	171	165	143	4.86	Yes	Yes	ATN	H	2	5	1.8	60	No	Yes	1	19	Neg	Neg	-	-	-
80	Veni	59	F	ADD	No	No	HN	-	4	3.2	80	78	137	6.7	No	No	-	C	-	-	1	42	Yes	Nil	1	32	Neg	Neg	-	-	-
81	Raghu	49	M	malaria	Yes	Yes	E,HN	8.6	9	9	231	231	143	5.37	No	No	ATN / AIN	H	2	14	2.6	22	Yes	No	2.7	50	No	Yes	Chronic interstitial Nephritis,	-	-
82	Johnson	35	M	ADD	Yes	No	-	14.3	5.6	5.6	130	150	139	4.2	No	No	-	C	-	-	2.4	46	No	No	0.9	26	No	No	-	-	-
83	Ganesh	33	M	sepsis	Yes	No	-	15.5	3.6	3.6	78	78	135	2.5	No	No	-	C	-	-	1.4	38	Yes	Yes	1	32	No	No	-	-	-
84	Kannan	27	M	sepsis	Yes	No	-	9.7	13.8	3	179	60	139	4.6	No	Yes	ATI	H	3	22	2.6	48	Yes	Yes	1.4	50	Nil	3+	-	-	-
85	Mogala	50	F	ADD	No	No	-	9.6	10.1	10.1	252	252	130	4.5	No	Yes	AIN	H	5	4	3.6	69	yes	Yes	1	30	Yes	Nil	Normal	No	No
86	Kandhan	44	M	malaria	No	No	-	8.9	4.6	4.6	110	100	138.6	4.67	Neg	Yes	-	C	-	-	2	20	No	Neg	1	28	Neg	Nil	-	No	No
87	Mageshwari	66	F	fever	Yes	Yes	-	7.7	8.5	4	166	68	137	2.1	Yes	Yes	-	H	4	8	1.7	48	No	Yes	0.9	30	Neg	Neg	-	No	No
88	Kaviraj	26	M	fever	Yes	Yes	H	9.7	13.6	3	170	170	137	3.8	Yes	Yes	AIN	H	5	4	3.6	38	Yes	Yes	1.4	50	No	Yes	-	No	No
89	Suresh	19	M	ADD	Yes	Yes	-	10.3	7.3	6.3	167	167	121	3.9	No	Yes	-	H	2	4	1.2	68	Yes	Yes	1	29	No	No	-	No	No
90	Mary	50	F	fever	Yes	Yes	-	9.1	8.7	7.1	301	301	118	5.5	No	Yes	AIN	H	5	4	3.9	100	Yes	Yes	3.4	100	Yes	Yes	Chronic Nephritis, Interstitial fibrosis	No	No
91	Beganraj	25	M	malaria	Yes	Yes	E,HY,J	7.9	11.9	5	209	195	133	3.7	Yes	Yes	ATN / AIN	H	2	15	3	40	Yes	Yes	1.1	30	No	Yes	Normal	No	No
92	Sambandam	54	M	ADD	No	No	-	10.8	9.8	9	226	173	133	5.5	Yes	No	-	H	4	5	2.4	52	No	No	1	28	No	Yes	-	No	No
93	Ramalingam	40	M	Pancreatitis	No	No	J	7.3	10.1	10.1	359	359	116	3.42	Yes	No	-	C	-	-	2	69	No	No	1	30	No	No	-	No	No
94	Senthil	49	M	leptospirosis	Yes	Yes	HY	7.8	5	4.5	130	121	138	4	Yes	Yes	-	H	2	5	1.8	73	No	No	1	30	No	No	-	No	No
95	Mayil samy	40	M	sepsis	Yes	No	-	11.4	11	6.4	182	140	138	4	Yes	No	-	H	2	3	1.2	47	No	Yes	1	30	No	No	-	No	No
96	Suganya	22	F	postpartum	Yes	Yes	J	6.5	6.2	4	126	80	137	3.1	Yes	Yes	TMA, Patchy cortical Necrosis	H	2	98	4	100	Yes	Yes	5	100	Yes	Yes	Interstitial Fibrosis,global glomerular sclerosis	No	No

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Analysis of causes risk factors and outcome in Acute Kidney Injury (AKIN - III)

Principal Investigator : Dr.T.Rajarajan

Designation : PG in D.M. (Nephrology)

Department : Department of Nephrology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI